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CHRONICLE OF THE WORLD HEALTH ORGANIZATION

TREPONEMATOSES : A WORLD PROBLEM

WORLD HEALTH ORGANIZATION
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The World Health Organization (WHO) is a specialized agency of the United Nations and represents the culmination of efforts to establish a single intergovernmental health agency. As such, it inherits the functions of antecedent organizations such as the Office International d'Hygiène Publique, the Health Organization of the League of Nations, and the Health Division of UNRRA.

WHO had its origin in the proposal made at the United Nations Conference held in San Francisco in 1945 that a specialized agency be created to deal with all matters relating to health. In 1946, representatives of 61 governments met at the International Health Conference, New York, drafted and signed the WHO Constitution, and established an Interim Commission to serve until the Constitution could be ratified by 26 Member States of the United Nations. The Constitution came into force on 7 April 1948, the first World Health Assembly met in Geneva in June 1948, and on 1 September 1948 the permanent Organization was established.

The work of the Organization is carried out by three organs : the World Health Assembly, the supreme authority, to which all Member States send delegates; the Executive Board, the executive organ of the Health Assembly, consisting of 18 persons designated by as many Member States; and a Secretariat under the Director-General.

The scope of WHO's interests and activities exceeds that of any previous international health organization and includes, in addition to major projects relating to malaria, tuberculosis, venereal diseases and treponematoses, maternal and child health, nutrition, and environmental sanitation, special programmes on public-health administration, epidemic diseases, mental health, professional and technical training, and other public-health subjects. It is also continuing work begun by earlier organizations on biological standardization, unification of pharmacopoeias, addiction-producing drugs, health statistics, international sanitary regulations, and the collection and dissemination of technical information, including epidemiological statistics.

* * *

The *Chronicle of the World Health Organization* is published in English, French, Spanish, and Chinese editions. It contains general information on the Organization, its principal activities, the meetings of its expert committees and other advisory bodies, as well as summaries of its main technical publications. Material from the *Chronicle* may be reproduced in the professional press, providing due acknowledgement is made.

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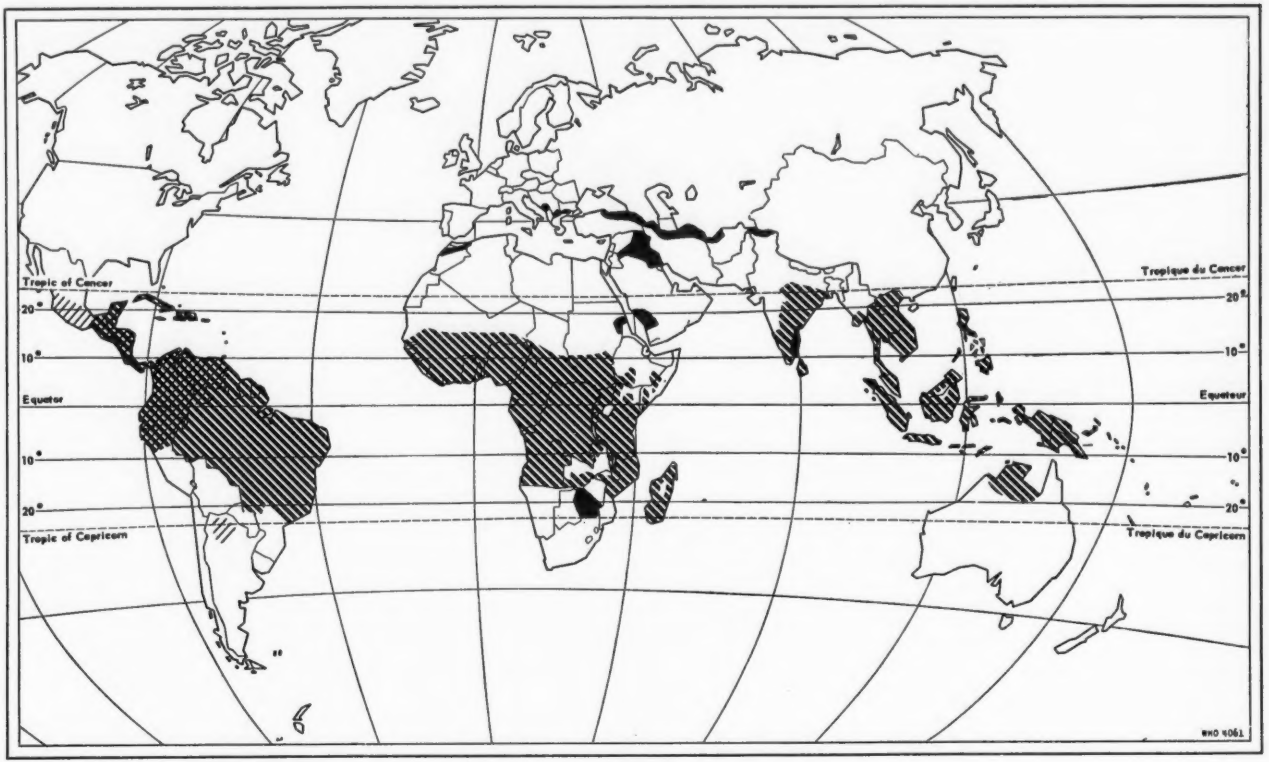
FIG. 1. GEOGRAPHICAL DISTRIBUTION OF THE NON-VENEREAL TREPONEMATOSES



Yaws *Pinta* *Endemic syphilis and similar conditions*

Venereal syphilis, which is more or less prevalent throughout the world, is not shown.

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Venereal syphilis, which is more or less prevalent throughout the world, is not shown.

CHANGING CONCEPTS IN THE EPIDEMIOLOGY AND CONTROL OF THE TREPONEMATOSES*

It has become widely recognized in recent decades that, despite the medical, technical, social, and economic advances of the past century, syphilis, yaws, and pinta represent a group of infections which continues to afflict a large proportion of the world's population (fig. 1). Regions where they are prevalent must be considered as " so many reservoirs of world infection, exactly as are foci of malaria or yellow fever ".[1] Furthermore, since the treponematoses are closely related to each other biologically and immunologically, and since the causative treponemes are all susceptible to penicillin, there is an increasing demand for a comprehensive world view of these infections as a group which would replace a narrow approach based on differences in clinical syndromes, mode of transmission, or other characteristics peculiar to one or another. From the point of view of public health and of communicable-disease control, there are definite advantages in the group concept, which has, in fact, gained acceptance by scientists, health workers, and administrators in many countries and has been the basis for practical measures taken to combat the treponematoses in different regions of the world over the past few years.

The study of the natural history of the treponematoses and their control require further definition of the relationship between the host and the parasite on the one hand, and the host and his physical, social, and economic environment on the other hand. Significant scientific developments and discoveries of recent years have added to our knowledge of these relationships, and the introduction of new and more effective health techniques has resulted in a basic reorientation in treponematoses control.

The isolation in the laboratory of a variety of strains and types of treponemes from various endemic areas of treponematoses in the world, the ability to maintain treponemes alive on artificial media for some time, the production in the experimental animal of relatively tissue-free and concentrated treponemal antigens, and the discovery of true immobilizing and agglutinating antibodies in the serum—as distinguished from the reagin type of " antibody " determined by usual serological methods—all these advances have greatly expanded our knowledge of the immunological and antigenic relationships among the different treponematoses.

Since there is no intermediate host to attack in the treponematoses, and since immunization procedures are impracticable at the present time, the principal approach to treponematosis control remains case-finding and treatment, which must be carried out simultaneously with efforts to raise the social, educational, and economic level of the population concerned.

* This special number of the *Chronicle* has been prepared by Dr. T. Guthe, Chief, Venereal Disease and Treponematoses Section, WHO, and Dr. R. R. Willcox, WHO Treponematoses Consultant.

[1] Quoted in Hudson, E. H. (1946) *Treponematoses*, New York, p. 116

In this domain, too, rapid strides have been made in recent years. The introduction of penicillin as an effective treponemicidal drug to replace the toxic arsenicals, and the development of repository penicillin preparations which will cure a high proportion of early infectious cases with a single injection, and which will also arrest the advanced disease, have made it possible for patients to be treated on an ambulant basis. Penicillin will protect against infection on actual exposure, and it is also effective when administered during the incubation period of a treponematosis. This has permitted the administration of the antibiotic to contacts without overt signs of treponematoses in an effort to sever the chain of infection as rapidly as possible, and this procedure has become an important epidemiological technique. The triple effect of penicillin—curative in manifest disease, preventive or "abortive" during the incubation period, and prophylactic against exposure to contagion—has therefore made it a medical agent which can be successfully used not only in individual patients in clinical practice, but also as an important public-health weapon for the general improvement of health conditions by means of mass control programmes wherever the treponematoses are highly prevalent.

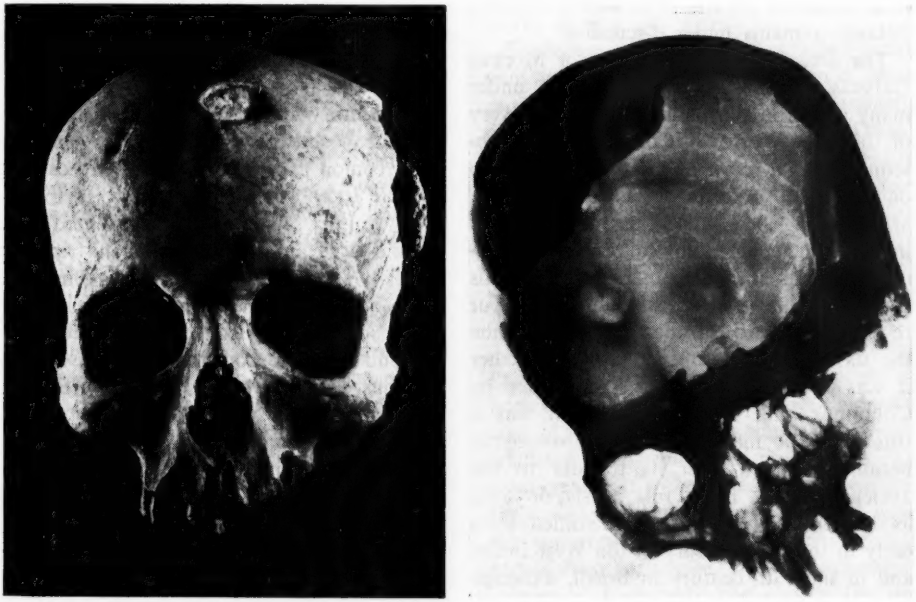
In the two articles which follow, the nature and extent of the treponematoses and the new methods for their control are considered in some detail, in order to provide background for subsequent sections on what has been accomplished and what remains to be done.

NATURE AND EXTENT OF THE TREPONEMATOSES

EPIDEMIOLOGICAL HISTORY

The question of the antiquity and origin of the treponematoses is one of the classical controversies of medical history. The finding of syphilitic bones from ancient peoples has given rise to various theories as to the geographical cradle of these infections, some investigators considering it to be in the Americas, others, in Europe, the Near East, or Africa. The recent discovery of possible bejel lesions in ancient bones found in the Eastern Mediterranean region has further emphasized this problem and has focused particular interest on the hypothesis of a single origin of the treponematoses. According to this hypothesis, one ancestral type of treponeme might, through the ages, gradually have adapted itself to widely differing environments in which climatic, ethnological, social, economic, and other factors have differently conditioned the

FIG. 2. ANCIENT SYPHILITIC SKULL FOUND IN IRAQ



The antiquity of the treponematoses has for many years been discussed by medical historians. Above is a skull, believed to date from the first half of the first millenium A.D., which bears evidence of gummous osteoperiostitis. This skull was discovered in 1939 near Zakho, Iraq, by the Government Archaeologist at the time, Seton Lloyd. In a recent study, made in connexion with a WHO/UNICEF bejel-control project, Drs F. Kail, of Vienna, and A. De Froe, Director of the Anatomical Department of the Royal College of Medicine, Baghdad, attribute the pathological changes in the skull to a treponematosis.

treponemes, their mode of spread, and the susceptibility of the host, with subsequent development of variations in the resulting clinical syndromes in man.

Whatever their geographical or biological origin, the treponematoses have been an international health problem throughout history, and epidemic outbreaks have been recorded for centuries. An infection similar to syphilis was known as " seamen's jealousy " in Chinese coastal towns in ancient times, and the Biblical plague of Moab has been identified as syphilis. To what extent it is possible to identify with syphilis an infection prevalent in eastern Europe many decades before the return of Columbus to Europe from the Americas at the end of the 15th century—and of which wooden illustrations of lesions are still to be seen in Cracow, Poland—remains under discussion.

The actual nature and extent of Morbus Gallicus, which spread epidemically under many names in Europe after the rediscovery of the New World by Columbus, and subsequently as a result of the travels of Vasco da Gama and other explorers to the Orient, are one of the classical examples of an international epidemiological problem. Medical historians are still debating whether this framboesia-like disease was introduced or re-introduced into Europe from Africa when the slave trade was opened up, or whether it was brought from the West Indies by Columbus and, indeed, whether it was a true syphilitic infection which subsequently became modified after its transfer to the ancient world. " True " framboesia, or yaws, as known today, was not identified until early in the 17th century in the West Indies and in the 18th century in Brazil, although a description was given as early as 1558 of a yaws-like disease among Indian children in Rio de Janeiro and other areas of Brazil, to which it may have been imported from Africa. Since then yaws has gradually become recognized as an ubiquitous plague throughout the tropical belt. The disease described as early as 1519 by Hernan Cortes during the period of Spanish conquest in the Western hemisphere was probably not yaws but the " blue stain disease ", or pinta, identified in recent years as another member of the treponematoses group.

There is historical evidence that many of the recorded epidemics of syphilis perpetuated themselves as extravenereal infections among children, and that this mode of transmission was often mixed with venereal transmission among adults. The sibbens, or " Scottish yaws ", of the 17th century, after the time of Cromwell, was apparently a mixture of venereal syphilis and such " syphilis innocens ", transmitted through drinking bowls, towels, and other utensils, and by suckling, sleeping with infected persons, etc. The last case of sibbens was reported in Britain a little more than one hundred years ago. The Norwegian " radesyge " of the 18th century has also been recognized as an extravenereal syphilitic disease, and the " spirocolon " of 19th-century Greece and Russia was of a similar nature. In the 18th century again, Canada suffered outbreaks of syphilis among Indian tribes at St. Paul's Bay and Lake Huron, where the disease was very prevalent among children.

Certain medical and social practices have undoubtedly also contributed to the spread of non-venereal syphilis over the centuries. An epidemic of syphilis is known to have resulted from cupping operations at the public baths in Moravia in 1587, and in France a midwife with a chancre on her finger infected 50 pregnant women in 1727—an event not uncommon before the invention of rubber gloves. In the days before artificial milks were used for baby-feeding, the wet-nurse also contributed to the spread of the disease. For example, more than 40 women and children and several men developed syphilis in an epidemic in France in 1752 as a result of infection among wet-

nurses who had developed nipple chancres through contact with syphilitic children. Other children in due course infected their mothers; and the husbands, at the end of the chain of transmission, acquired the disease venereally from their wives. There are several accounts of the early periods of smallpox vaccination in which the arm-to-arm technique of vaccination is known to have resulted in the direct spread of syphilis from persons with infectious lesions. The introduction of the eustachian catheter was also followed by a number of cases of transmitted syphilis. Chancres resulting from circumcision procedures have frequently been reported in the literature. And, in modern times, blood transfusion and the tattooer's needle have occasionally been responsible for the transmission of syphilis.

THE PRESENT PROBLEM

The principal treponematoses—syphilis, yaws, and pinta—are infections resulting from the interplay of the environment, the human host, and the specific micro-organism concerned, which may be *Treponema pallidum*, *T. pertenue*, or *T. carateum*. The fact that all the treponematoses except sporadic syphilis are essentially non-venereally transmitted has been held to account for some of the differences (i.e., non-occurrence of systemic cardiovascular and neurological involvement) between them and venereal syphilis; but it does not explain the variations among the other treponematoses themselves.

In contrast to those of syphilis, the treponemes of yaws and pinta are apparently not transmitted sexually, and the reciprocal partial immunity among the treponematoses, which may represent a natural barrier to the introduction of venereal syphilis in areas in which the non-venereal treponematoses are prevalent, will gradually disappear once the latter have been controlled. However, the ultimate pattern of venereal transmission may, even in developed countries, revert to an extravenereal pattern, given a return to conditions of poverty, overcrowding, war, or a combination of factors which are conducive to the non-venereal mode of transmission. Thus, local outbreaks of asexual syphilis among children were recorded in Budapest in 1948 [2] and in Chicago in 1949,[3] and were, in both instances, attributable to unfavourable social conditions. On the other hand, examples may be cited of males from underdeveloped areas who have acquired venereal syphilis on visits to large cities and who have venereally infected their wives on their return to their homes; the wives, in turn, have infected the children non-venereally; and this has given rise, under favouring environmental conditions, to an epidemic of non-venereal syphilis among the children in the area.

Epidemic or endemic syphilis cannot continue to exist by non-venereal transmission unless numerous environmental factors further this form of spread. There is evidence that, with improvement in hygienic conditions and with general social and economic advancement, the non-venereal type of syphilis has died out in many parts of the world, although important areas where non-venereal transmission predominates still exist in Europe, the Middle East, Asia, Africa, the Americas, and the Western Pacific. Experience in recent years has shown, however, that active communicable-disease-control programmes, with emphasis on health education, environmental sanitation, and mass treatment with penicillin, can accelerate the social and economic process by which the suppression of endemic syphilis—or of any of the other non-venereal treponematoses—may be furthered. And, once the non-venereal treponematoses have been sup-

[2] Fèjer, E. (1948) *Orv. Lapja*, 4, 616

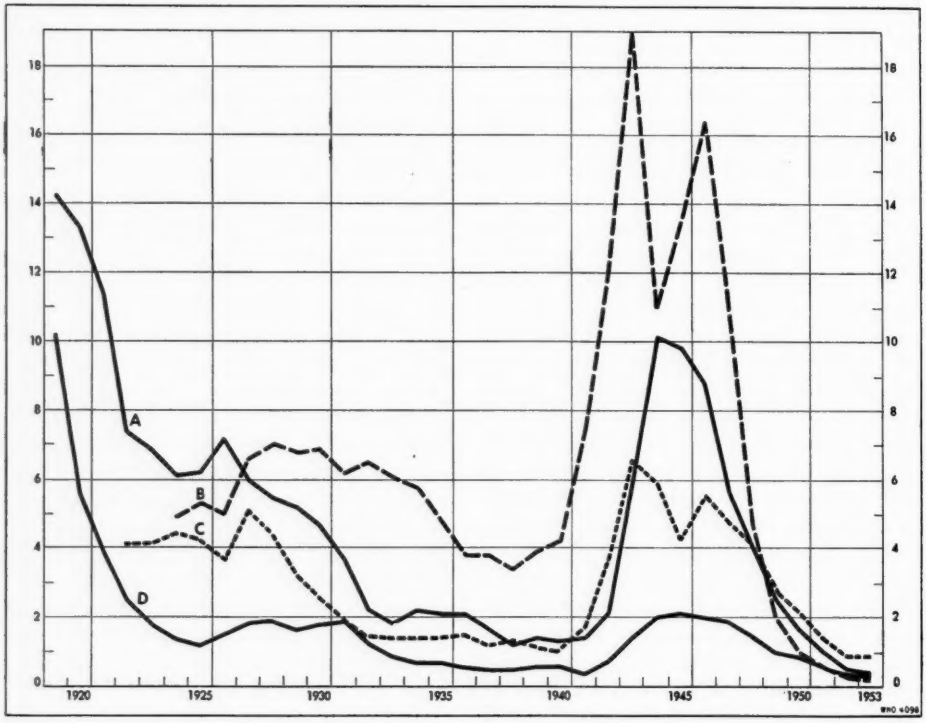
[3] Eisenberg, H., Plotke, F. & Baker, A. H. (1949) *J. vener. Dis. Inform.* 30, 7

pressed in populations with low socio-economic standards, emphasis will shift to new problems of disease control.

VENEREAL SYPHILIS

Attempts to secure detailed information concerning the actual extent of the problem of venereal syphilis throughout the world suggest that at least 20 million cases exist, although the data available are scattered and not always reliable. It is not always possible, though desirable, for each area and country to be fully aware of its treponematoses problem and to include data on infectious syphilis, at least, in local and national health statistics. Even an approximate estimate of the disease problem to serve as a basis for planning control programmes is not always obtainable. In applied serology there may also be difficulties, leading to an exaggerated opinion of the prevalence of syphilitic infection in tropical and semi-tropical areas owing to the fact that seropositivity may be the result of one of the other treponematoses

FIG. 3. ANNUAL CASES OF PRIMARY AND SECONDARY SYPHILIS PER 10,000 POPULATION REPORTED IN DENMARK, FINLAND, NORWAY, AND SWEDEN, 1919-53



Ordinates : rate per 10,000

A — Denmark *B — Finland* *C — Norway* *D — Sweden*

(true seropositivity) or of false-positive reactions caused by non-treponemal infections.

In spite of these limitations, fairly reliable data are available for some countries where venereal-disease control has been organized for some time, as, for instance, in the Scandinavian countries, where such activities date back to the 17th century. In these and similar areas where it has been possible to measure trends over a period of time, it has been observed that venereal syphilis remains predominantly an urban disease in "normal" times. It invades rural areas during times of poverty, war, and occupation, and with migrating populations. Following every major war, its prevalence decreases with a return to normal economic and social conditions and with a stabilization of the population. This decline in prevalence may be accelerated by systematic case-finding, by adequate treatment of cases, and through educational efforts. The incidence of early syphilis in the Nordic countries is illustrated for the period covering both World Wars in fig. 3, and it is interesting to note the syphilis epidemics which occurred there during the war periods and in the immediate post-war years. The drop in the incidence of early infections was similar in Denmark and Norway after both the First and the Second World Wars; after the Second, however, the rapid decline persisted, and the incidence reached a minimum level without the long, secondary, drawn-out process which spanned almost two decades after the First World War.

In post-war Germany, where military occupation, instability of the population, and many other factors might have tended to maintain the incidence of venereal diseases at a relatively high level, a continued decrease in the rate of early syphilis has been experienced following a maximum incidence in all three western occupied zones in 1947. A similar rapid decline seems to have followed the post-war peaks noted in Canada, Finland, France, Italy, Poland, the United Kingdom of Great Britain and Northern Ireland, and several other countries, although it is difficult to appraise the situation accurately since the statistical information is sometimes based only on patient-loads at outpatient departments of venereal-disease clinics, which may not directly reflect quantity, but rather indicate a general trend in a given area.

The trend of syphilis incidence in the USA over the past few years is of considerable interest, particularly in the light of the evaluation, made by the WHO Syphilis Study Commission to the USA in 1950,[4] of the venereal-disease-control programme there after the introduction of penicillin. This trend is illustrated in fig. 4, and it will be seen that a rapid decline occurred in early infectious syphilis after penicillin had been introduced on a considerable scale.

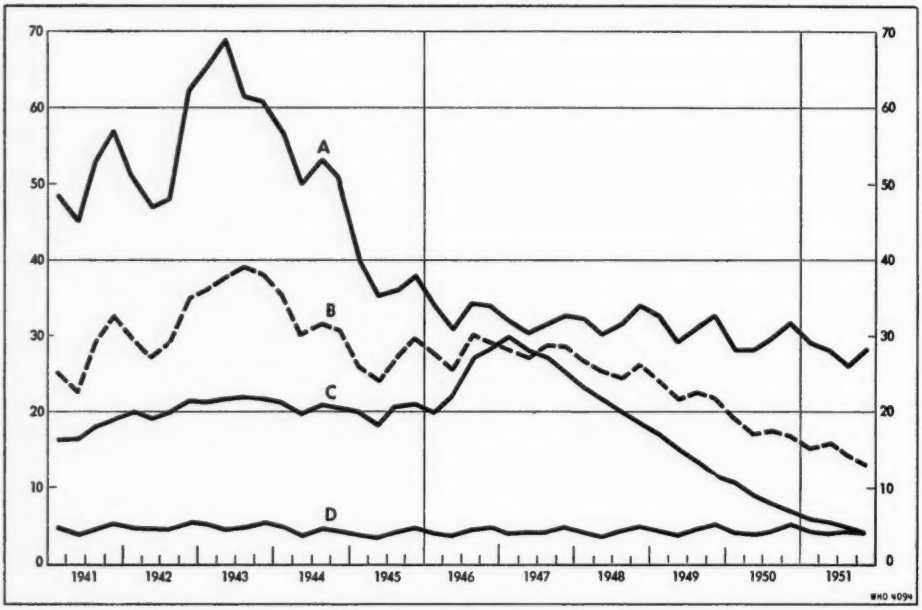
It is an inherent feature of the problem of venereal syphilis that, regardless of general prevalence, geographical distribution, peace, or war, the majority of early cases occur in the productive age-groups, with a preponderance among young females, who are often infected at an earlier age than the males. This age and sex distribution may be seen in table I.

Despite the rapid decline in the incidence of early syphilis in several western countries after the Second World War, foci have continued to persist in some areas or among certain population-groups in those countries. Relaxation of venereal-disease-control efforts, misconception concerning the ease of modern therapy, and lack of adequate maintenance of case-finding and follow-up work may even lead to recrudescence of the disease. It has recently been reported that in 15 States of the USA the incidence of syphilis increased in 1953.[5] Long-range planning and sus-

[4] *Wld Hlth Org. techn. Rep. Ser.* 1950, 15

[5] Cutler, J. C. (1953) Presentation before annual meeting of American Society for Investigative Dermatology

FIG. 4. CASES OF ACQUIRED SYPHILIS IN THE USA (STATES AND TERRITORIES), BY FISCAL-YEAR PERIOD, 1941-51 *



Abscissae : fiscal-year quarters
Ordinates : thousands of cases

A — Late and late latent
B — Early latent
C — Primary and secondary
D — Congenital

tained efforts are therefore necessary in any treponematosis-control programme. As the reservoir of early infectious treponematosis is brought under control, by extensive case-finding and treatment, the emphasis shifts to the late and latent stages of the disease, the combating of which becomes a desirable public-health objective. This is the case in some of the more developed countries in which the former objective has begun to be attained.

TABLE I. AGE DISTRIBUTION OF 4,145 REPORTED CASES OF PRIMARY AND SECONDARY SYPHILIS IN NEW YORK CITY, 1943

Age (years)	Number with primary or secondary syphilis			Percentage with primary or secondary syphilis		
	males	females	total	males	females	total
under 15	4	14	18	0.1	1.1	0.4
15-19	306	305	611	11.4	20.9	14.8
20-24	795	543	1,338	29.6	37.3	32.4
25-29	511	288	799	19.0	19.8	19.3
30-34	365	152	517	13.6	10.4	12.1
35-39	253	76	329	9.4	5.2	8.0
40-44	195	37	232	7.3	2.5	5.6
45-49	129	21	150	4.8	1.4	3.7
50-54	71	15	86	2.6	1.0	2.1
55 and over	59	6	65	2.2	0.4	1.6
Total	*2,688*	*1,457*	*4,145*	*100.0*	*100.0*	*100.0*

* Known military cases are excluded.

From the international point of view, the extensive reservoir of syphilitic infection remaining in vast regions in several parts of the world is, on the other hand, of greater significance, particularly in areas where facilities for diagnosis and treatment are limited and where venereal-disease-control activities have not previously been organized on an appreciable scale. For example, the prevalence of venereal syphilis has been reported [6] to vary from 14.1% to 32.9% of the population in certain areas of Africa; syphilis surveys in South-East Asia have shown a prevalence of seropositivity ranging from 0.6% to 31% in different population-groups in Afghanistan, from 2.4% to 25.4% in Burma, from 0.5% to 11.9% in Ceylon, and from 5% to 50% in India; in the Eastern Mediterranean region, recent extensive surveys have shown a range in Egypt of from 0.2% to 27%, in Ethiopia of from 4.2% to 82%, and in Saudi Arabia of from 8% to 22%; and surveys of large population-groups in the Americas have shown a range of from 12% to 15%. There can therefore be no doubt that millions of cases of syphilis remain in these areas.

It has been found that the prevalence of venereal infections, particularly of syphilis, is relatively higher in ports than in inland cities, both in developed and in underdeveloped areas. This raises the special problem of the possible transfer of infection from one country to another, and has therefore been the object of particular international attention, which is exemplified in the Brussels Agreement of 1924 for the treatment of seafarers in foreign ports (see page 89).

In short, although there has been an initial significant decrease in early venereal syphilis in some parts of the world since the Second World War, the problem of syphilis continues to be a health hazard in many other regions, at a time when rapid transport by land, sea, and air is now available, when desert treks and migrations have increased considerably in volume, and when commercial intercourse between countries is accelerating under the vast economic development and expansion programmes in many underdeveloped areas.

[6] Unpublished reports of WHO advisers or consultants (1949-52)

NON-VENEREAL TREPONEMATOSES

The decline in early, venereally acquired syphilis in some parts of the world in recent years has called increasing attention to the continued existence of endemic, hyperendemic, and epidemic areas of non-venereal syphilis, yaws, and pinta. Although precise statistics are still lacking, there is a growing realization of the significance of these infections as public-health problems; and survey and control programmes—sometimes with international assistance—have begun to give some idea of their widespread distribution and considerable prevalence.

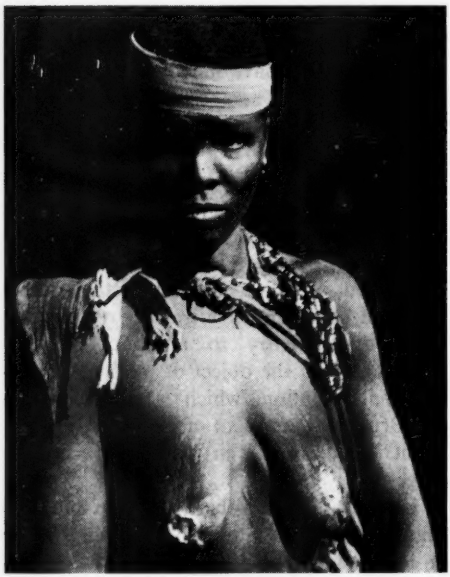
Endemic syphilis and similar conditions

Syphilis has remained an ordinary communicable disease in several areas of the world, transmitted non-venereally by direct contact and by indirect transfer of *T. pallidum* among children and adolescents through their play, and by drinking vessels and common eating and other household utensils under primitive, crowded, substandard conditions of living. Non-venereal syphilis in its endemic form is an infection with epidemiological features which have furthered its spread primarily among children to such an extent that the epidemiological term "endemic syphilis" has by common usage become identified with the mere presence of the clinical syndrome most frequently found as the first sign of this childhood disease—namely, oral mucous patches. In Bosnia, Yugoslavia, such syphilis among children was widespread until very recently; and, in

FIG. 5. EXAMPLES OF MODES OF TRANSMISSION OF NON-VENEREAL TREPONEMATOSES

A — Common use of drinking vessel (the "ibrik") in Bosnia: a method of spread of endemic syphilis
(E. I. Grin, Sarajevo)

B — Transmission of yaws by direct skin contact of body surfaces of African miners
(C. J. Hackett, London)



C — Chancre of the breast in mother nursing dichuchwa-infected child having mucocutaneous lesions in the oral region
(J. F. Murray, Johannesburg)

FIG. 6. EARLY LESIONS IN ENDEMIC SYPHILIS

Oral mucous lesions of non-venereal syphilis (Bosnia)
(E. I. Grin, Sarajevo)

Similar lesions in "njovera" (Southern Rhodesia)
(R. R. Willcox, London)

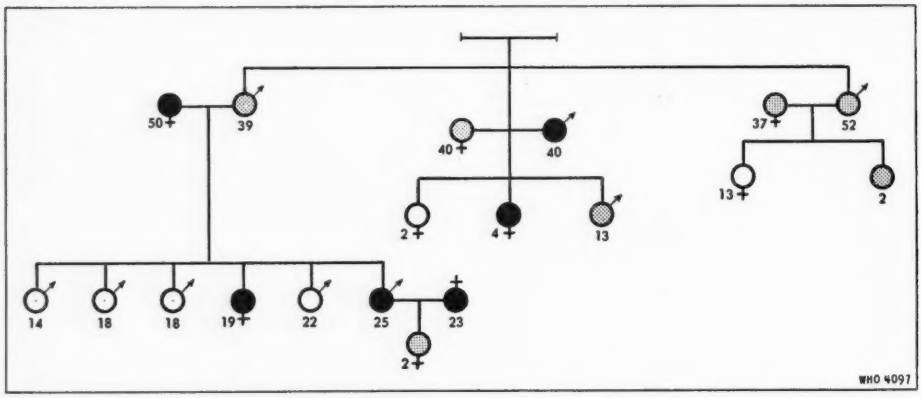
the neighbouring republic of Serbia, a more mixed venereal and non-venereal type of infection was found. Prior to the mass treatment campaign of 1948-52, there were an estimated 100,000 cases (5%) among the two million inhabitants of the rural areas of Bosnia. The high prevalence of infection among children and in the lower age-groups in this area is illustrated in table II.

There are no essential differences between the tegumentary lesions of endemic syphilis and those of sporadic, venereally acquired syphilis in adults, and the symptomatology of both includes gummatous destruction of the skeleton. It is contended that cardio-vascular and neurological involvement is present in the later stages of both. But the rarity of primary lesions and of congenital manifestations is one of the characteristics of endemic syphilis; and, since they occur in the early age-groups, their incidence is different from that found in an environment where a venereal mode of transmission prevails and where sexually mature adults, rather than children, represent the population at risk.

TABLE II. NEW CASES OF ENDEMIC SYPHILIS BY AGE-GROUPS IN A BOSNIAN COMMUNITY

Age (years)	Population	Early infectious cases	Cases per 1,000 of population
0-10	860	120	139.5
11-20	1,051	71	67.6
21-30	842	31	36.8
31-40	432	2	4.6
over 40	724	20	27.6
Total . . .	*3,909*	*244*	*62.5*

FIG. 7. ENDEMIC SYPHILIS IN A HOUSEHOLD OF 19 MEMBERS (5 FAMILIES) IN BOSNIA, 1951



● *Early secondary lesions* ◍ *Latent* ○ *Clinically and serologically negative*

Figures indicate the age of the individual.

This difference is at least partially explicable on epidemiological and immunological grounds; there is no evidence of a true difference in the strain, virulence, or tissue-tropism of *T. pallidum* in endemic or venereal syphilis.

Studies of the prevalence of endemic syphilis in crowded households with little living space show that there is a considerable likelihood of many family members' becoming infected. The age and sex distribution in a typical household of this sort, where two-thirds of the persons living under the same roof were infected, is shown in fig. 7.

In small communities, the daily contact among inhabitants is usually more intense than in larger villages; and it has been found that, the more compact the community, the higher the infection-rate, since there are more opportunities for the transfer of treponemes. A survey of 322 Bosnian villages, illustrated in the following tabulation, shows a progressive decrease in the infection as the population in the villages increases :

Village population	*Infected, %*	*Village population*	*Infected, %*
less than 200	22.5	400-600	12.6
200-400	16.2	over 600	9.1

Since the exhaustive studies by von Düring[7] on spirochaetosis in Mesopotamia and westward to the Mediterranean were made in 1896, a condition quite similar to, if not identical with, endemic syphilis has been described under the name of " bejel " by many investigators in various other parts of the Eastern Mediterranean region. Apparently the condition is of some antiquity; but, whatever its origin, it is found almost exclusively among Arabs in remote, primitive, desert villages in Iraq, Syria, and the Hashemite Kingdom of the Jordan, where it has for many decades been recognized by the Bedouin as a common childhood and family infection. Epidemiological and pathological descriptions of endemic syphilis and bejel have also been given in recent years by workers in Iran, Saudi Arabia, and other Eastern Mediterranean areas. It has been estimated that this type of infection may afflict a million or more persons in this region.

The early onset and the age and sex distribution of bejel are similar to what is found in endemic syphilis (see table II).

[7] Düring, E. von (1918) *Arch. Derm. Syph. (Berl.)*, **61**, 3

The clinical resemblance of the initial stages of bejel to those of endemic syphilis is striking and has been described by a number of investigators.[8, 9, 10] The lesions are usually confined to the skin, mucous membranes, and skeleton. Primary sores are extremely rare, and involvement of the cardiovascular or nervous system in the later stages has not been demonstrated with certainty in large series of patients, although random reports suggest that it may occur. It has been stated that the fundamental distinction between endemic non-venereal syphilis and bejel or bejel-like conditions lies in the presence or absence of systemic neurological and/or cardiovascular involvement in the later stages of the disease. It is still not certain whether such involvement in endemic syphilis may not be attributable to cases of venereal origin in areas with mixed venereal and non-venereal syphilis; it is also debated whether the isolated cases of similar involvement in bejel are due to the same cause.

Early reports of possible congenital bejel have not been confirmed where it has been possible to follow for any length of time children born of women seropositive at pregnancy. Darkfield-positive mucous patches and skin lesions, including anogenital condylomata, are common early manifestations. Most patients go into latency after the early stages, with subsequent development of late lesions of the skin and bone.

In bejel, as well as in yaws and possibly in endemic syphilis, there is a seasonal increase in the attack-rate with the coming of summer and the warmer weather. Proximity to marshes or lakes may be among the physiographic factors facilitating the spread of infection in areas with poor hygienic standards, although such factors appear to play a smaller role as environmental sanitation improves. This has been demonstrated[11] in adjacent Iraqi villages inhabited by Kurds and Djibours, respectively, and where the conditions are remarkably different.

A treponemal infection called " njovera ", and closely resembling endemic syphilis and bejel, has recently been described[12] in Southern Rhodesia among the Karanga people in Africa. It is contended that bejel and njovera are identical and that both are, in fact, non-venereal endemic syphilis. " Dichuchwa " has been described by McArthur,[13] Murray et al.,[14] and others as another endemic extravenereal treponematosis among the Bantu people of Bechuanaland; it appears to be mixed with venereal syphilis. In both these non-venereal treponematoses—njovera and dichuchwa—primary lesions are rarely seen except as " throw-back ", transpositional lesions where a nipple-sore develops in the mother from her infected child (fig. 5 c, page 48). The combination of darkfield-positive mucous lesions and condylomata is common in both conditions, which are otherwise characterized by the typical history of infection in childhood : natural regression or rapid response to minimal treatment, typical gummatous lesions in later life, and the occurrence of the infection as a family and household disease. Definite evidence has not been presented that cardiovascular or neurological involvement exists in either njovera or dichuchwa.

These are examples of non-venereal treponematoses recently identified in Europe, the Middle East, and Africa. There is increasing evidence of the existence in various other areas of the world of similar foci of endemic non-venereal syphilis or bejel-like conditions, bearing many strange names. Such conditions have been identified in

[8] Hasselman, C. M. (1938) *Arch. Derm. Syph. (Chicago)*, **38**, 837

[9] Hudson, E. H. (1938) *Amer. J. trop. Med.* **18**, 675

[10] Willcox, R. R. (1953) *Glasg. med. J.* **34**, 281

[11] Csonka, G. W. (1953) *Brit. J. vener. Dis.* **29**, 95

[12] Willcox, R. R. (1951) *Lancet*, **1**, 558

[13] McArthur, D. C. (1923) *Amer. J. Syph.* **7**, 3

[14] Murray, J. F., Merriweather, A. M., Keen, P. & Sachs, S. B. (1952) *Med. ill. (Lond.)*, **6**, 407

FIG. 8. TREPONEMATOSES IN BECHUANALAND

Gross nasopharyngal ulceration of five months' duration with history of attack of dichuchwa, in childhood, which regressed spontaneously

(J. F. Murray, Johannesburg)

Macedonia, Greece, Turkey, Lower Mongolia, Tibet, Tahiti, India, Saudi Arabia, Niger (French West Africa), and the Americas. They appear to be clinically and epidemiologically similar, and are at least closely related, if not identical. It is suggested that an appreciable percentage of the population is affected in many areas and that the number of people at risk is in the millions.

Yaws

Yaws is conditioned in its distribution by physiographic, economic, sanitary, and other environmental factors and is highly prevalent in, and almost exclusively confined to, the belt between the Tropic of Capricorn and the Tropic of Cancer (see fig. 1, page 38). It is estimated that there are some 50 million cases of yaws in all its forms in the world.

In the Americas, yaws is found in the northernmost countries of South America, to only a limited extent in Central America (Panama), and most widely in the Caribbean area. It has been estimated that there are some 350,000 cases of yaws in Brazil, where it exists in almost every State, although it is not a major problem in the southern part of the country. The prevalence in 1948 in British and French Guiana was 26.4 and 41.3 per 100,000 of the population, respectively. It is a health problem in rural areas of Venezuela, Colombia, and Ecuador. Probably the highest prevalence of yaws in the world existed, until recently, in Haiti, where more than 50% of the population were afflicted. There are reservoirs in the Dominican Republic, Jamaica, and Tobago.

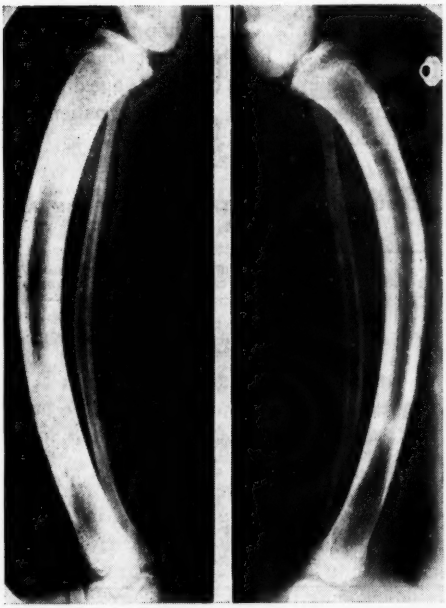
Africa has the largest single continental reservoir of yaws known. Conservative estimates suggest that there are about 25 million cases of yaws in tropical Africa.

In South-East Asia, yaws is prevalent throughout Indonesia and the peninsula comprising Malaya, Thailand, and the States of Indo-China. Its prevalence in Thailand and Indonesia, where an estimated 12-15 million cases existed until recently, is sharply declining under the mass control campaigns now under way in those countries. The disease is also found in scattered pockets in southern India, Burma, and Ceylon.

In the Western Pacific region, yaws is encountered in many islands. It is found in the Philippines, New Guinea, and in the Gilbert, Ellis, Solomon, and other island groups, sometimes with a very high incidence. In Australia, the irkintja, or " boomerang leg ", among aborigines has been identified as yaws by Hackett.[15]

[15] Hackett, C. J. (1936) *Trans. roy. Soc. trop. Med. Hyg.* 30, 137

FIG. 9. BONE LESIONS IN YAWS



X-ray of "boomerang leg" observed among the aborigines of Australia.

(C. J. Hackett, London)

Yaws is a disease of rural areas "at the end of the road", and its incidence is paradoxically associated with the presence of water. It is, on the one hand, recognized that, in remote, tropical, rural villages with little water and limited cleanliness, the attack-rate of yaws is higher than in areas where water can be used more freely for general domestic purposes. On the other hand, the attack-rate increases significantly with the increased humidity of the rainy season. Under crowded and primitive conditions, the infection is easily transmitted by direct contact with secretions from infectious lesions, and probably also by indirect contact.

It is primarily a disease of childhood and adolescence. Its early onset is illustrated in fig. 27, page 106. The primary sore, or "mother yaw", often appears at the site of an abrasion, and is seen on exposed parts of the body, such as legs, arms, buttocks, or face. The initial lesions are roughly analogous to those in syphilis, but those representing the different stages of yaws may appear far closer to each other in time than

FIG. 10. ULCERATING TREPONEMATOSIS LESION COVERED WITH FLIES

Purulent secondary infections result from flies under unhygienic environmental conditions.

(F. Kail, Vienna)

the corresponding lesions in syphilis. Generalized secondary framboesides of the skin and lesions of the bone and joints may appear a few weeks after the initial lesion and persist for years, with intermittent periods of apparent recovery and relapse, if no treatment is given. The plantar lesions known as " crab yaws " are particularly painful. Tissue destruction takes place earlier and is a more constant feature in yaws than in syphilis. Mutilation, permanent invalidism, and incapacitation for work result in many instances. (See fig. 9 and 23.)

Although standard scientific classification of yaws lesions and a generally agreed nomenclature must await future action by an international group of experts, the First International Symposium on Yaws Control, convened by WHO in 1952, considered the immediate need for a simple, general grouping of lesions as a basis for yaws-control projects in the field, where lesions are often recorded by auxiliary personnel with limited medical training ; this grouping was subsequently approved by the WHO Expert Committee on Venereal Infections and Treponematoses.[16]

The true clinical course of yaws and the relationship between its stages are still under discussion.

Pinta

Pinta is a public-health problem in Mexico and Colombia, where approximately 2% of the population are affected—with an estimated 250,000 cases in the former and 400,000 cases in the latter. It is also found in Argentina, Chile, Cuba, the Dominican Republic, Ecuador, Haiti, Peru, Venezuela, and certain of the islands of the Antilles. It is not with any certainty known to exist in areas outside the Americas. Cases reported in other regions are more likely to be " pintide yaws ".

[16] *Wld Hlth Org. techn. Rep. Ser.* 1953, **63**, 33

T. carateum was established[17] as the causative agent of pinta in 1938. The disease is essentially one of childhood and is contracted early in life by direct and indirect contact with infectious cases. Its age distribution among series of untreated patients is illustrated in table III.

TABLE III. AGE DISTRIBUTION OF PINTA IN 665 MEXICAN INDIANS, 1952 *

Age (years)	Number of cases	Percentage of total infected
1-5	60	9.0
6-10	143	21.5
11-15	134	20.1
16-20	115	17.3
21-30	141	21.2
31-40	47	7.1
41-50	17	2.6
51 and over	8	1.2
Total . . .	*665*	*100.0*

* Based on material from Rein, C. R., Kitchen, D. K., Marquez, F. & Varela, G. (1952) *J. invest. Derm.* **18**, 137

Clinical manifestations are confined to the skin, and there is no certain evidence of congenital disease or of systemic cardiovascular or neurological involvement. Primary pinta lesions are followed by secondary manifestations with localized and sometimes extensive dissemination, as in syphilis. These give rise to copper-coloured pigmented areas which turn slate-blue. Some of the pintides undergo depigmentation over extensive areas of the body surface, becoming " late " or " white " pinta, which represents the terminal stage of the disease. The changes proceed in an irregular fashion, with recurrence of secondary lesions periodically in the late stages of the disease and with a possible intermingling of all varieties of dyschromia, hypochromia, and achromia in the same patient.

[17] Saenz, B., Grau Triana, J., & Alfonso Armenteros, J. (1938) *Arch. intern. Med.* **4**, 112

The manifestations of pinta are usually not physically incapacitating in the same way as those of syphilis, bejel, and yaws. Pinta may, however, become a social and a mental health problem : the sufferer from pinta of the blue, white, or mixed varieties may feel stigmatized and may sometimes not be accepted for employment in urban areas. In this respect the infection is a hindrance to the full utilization of peasant labour in growing industrial areas or where there is urban development.

NEW METHODS OF CONTROL

PENICILLIN AS A PUBLIC-HEALTH WEAPON

The management of treponematoses has been completely revolutionized since penicillin was first shown, more than ten years ago, to be effective against this class of infection,[18, 19] and since it was first successfully used by Mahoney and his co-workers [20] against venereal syphilis and then by other workers against endemic non-venereal syphilis,[21] yaws,[22] bejel,[23] and pinta.[24] Numerous investigators have demonstrated that the use of penicillin brings about rapid disappearance of early lesions, healing of lesions of the skin and mucous membrane, reversal to seronegativity and, in late manifestations, an effect equal to, or better than, that observed with metal chemotherapy. Long-term studies in syphilis [25] have shown that, when *adequate* amounts of penicillin are used, adjuvant therapy with arsenicals and bismuth will not improve the clinical and laboratory results (fig. 12, page 57).

T. pallidum is one of the most sensitive micro-organisms known. As little as 0.0025 unit of penicillin per ml of serum will immobilize 50% of a given number of treponemes within 16 hours; yet, in order to kill treponemes, they must be exposed to penicillin in the blood and tissues for a longer time than most other micro-organisms. After intramuscular injection, the concentration of penicillin in the tissues increases in a definite relationship to that in the serum, and the ultimate concentration in the infected organs is not appreciably lower than that in the circulating blood. The amount of penicillin required to kill the treponemes in the host depends on their number, and it is believed that they are most numerous in the secondary stage of syphilis before the immunobiological processes have come fully into play and the refractory stage has been reached. It has been established that the " minimum theoretical therapeutic " penicillin concentration in the blood is approximately 0.03 unit per ml. Although it has been calculated that such a concentration maintained for 96 hours should be sufficient, this treponemicidal level should be maintained for approximately one week in primary and two weeks in secondary syphilis to avoid the risk of any residual treponemes' recuperating and multiplying anew. It has not been shown that the treatment of syphilis is rendered more effective by maintaining a higher penicillinaemia or

[18] Liverpool School of Tropical Medicine, 44th Annual Report August 1, 1942—July 31, 1943, p. 9
[19] Lourie, E. M. & Collier, H. O. J. (1943) *Ann. trop. Med Parasit.* 37, 200.
[20] Mahoney, J. F., Arnold, R. C. & Harris, A. (1943) *J. vener. Dis. Inform.* 24, 355
[21] Grin, E. I. (1953) *Epidemiology and control of endemic syphilis : report on a mass-treatment campaign in Bosnia,* Geneva (*World Health Organization* : *Monograph Series* No. 11)
[22] Findlay, G. M., Hill, K. & Macpherson, A. (1944) *Nature (Lond.),* 154, 795
[23] Akrawi, F. (1949) *Brit. J. vener. Dis.* 25, 115
[24] Rein, C. R., Kitchen, D. K., Marquez, F. & Varela, G (1952) *J. invest. Derm.* 18, 137
[25] Shafer, J. R. & Usilton, L. J. (1954) *Bull. Wld. Hlth. Org.* (in press)

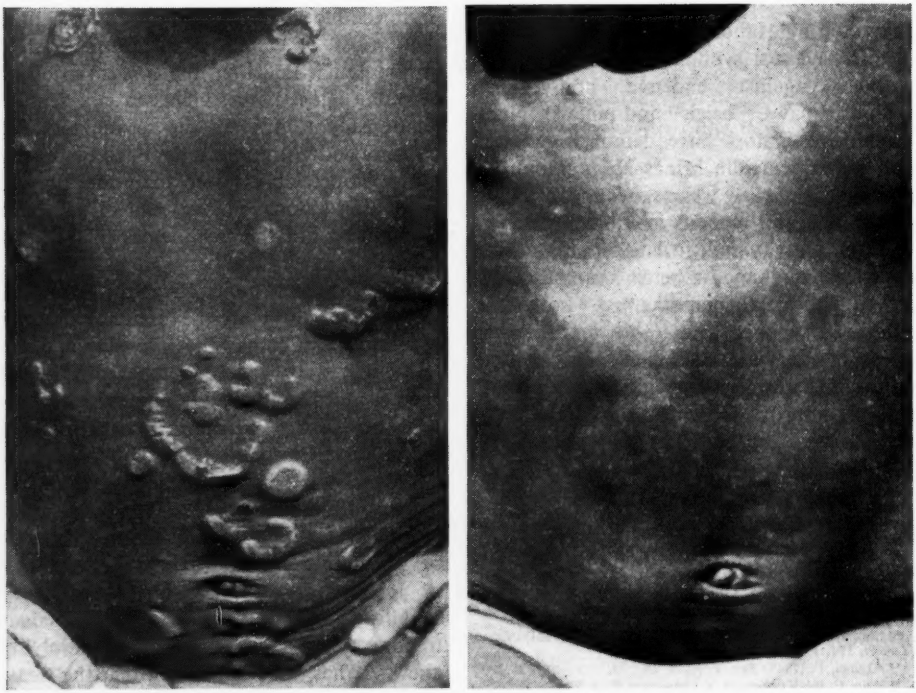
that there is any advantage in high, intermittent, peak penicillin concentrations in the serum or tissues.[26] The early clinical and laboratory studies were made particularly on syphilis, but several subsequent studies confirm that there are no essential differences in this respect between syphilis and the other treponematoses, although certain minor variations have been observed in penicillin sensitivity among strains of treponemes isolated from endemic syphilis, bejel, and yaws.

The required penicillinaemia of long duration can be obtained with different penicillin salts and preparations, provided that the dosage is adjusted to their characteristics and that the variables in the time-dose relationship of penicillin therapy are taken into account. Aqueous penicillin G injected several times daily during treatment necessitates hospitalization and is impractical for physician, hospital, and patient alike. It will give intermittently high blood-concentrations, and a large proportion of the penicillin will be wasted. The introduction by Buckwalter & Dickison[27] of a preparation of procaine penicillin G in oil with aluminium monostearate (internationally known as PAM) provided a practical product which gives a penicillinaemia of long duration when administered

[26] Eagle, H., Fleishmann, R. & Levy, R. (1953) *J. Lab. clin. Med.* **41**, 122

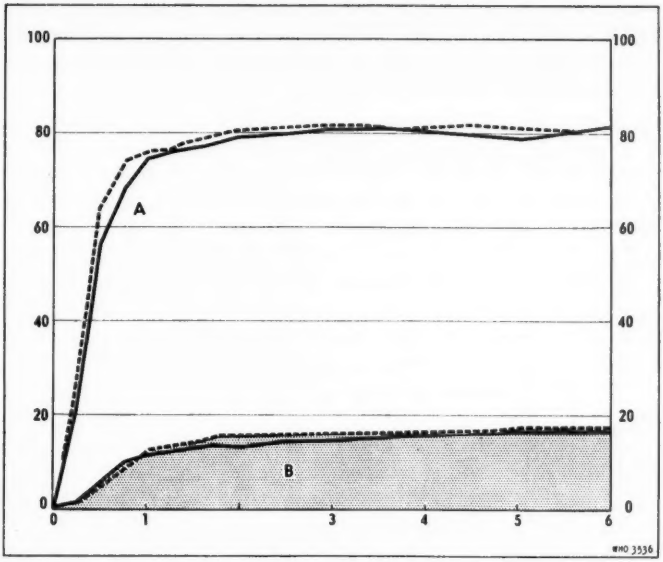
[27] Buckwalter, F. H. & Dickison, H. L. (1948) *J. Amer. pharm. Ass.* **37**, 472

FIG. 11. IMMEDIATE EFFECT OF LONG-ACTING PENICILLIN (PAM) IN THE TREPONEMATOSES



Maculopapular secondary lesions of yaws before, and three weeks after, injection of 1.2 mega units of PAM
(K. R. Hill, Kingston, Jamaica)

FIG. 12. PENICILLIN ALONE COMPARED WITH PENICILLIN PLUS ARSENOXIDE AND BISMUTH IN THE TREATMENT OF SECONDARY SYPHILIS



Abscissae : years of observation
Ordinates : cases (%)
— *Penicillin alone (3.2 mega units)*
--- *Penicillin (2.8 mega units) plus arsenoxide (300 mg) and bismuth (600 mg)*
A — Seronegative
B — Re-treated

in one or a few intramuscular injections. This has made for a more rational utilization of penicillin from the point of view both of therapy and of economy. It is, however, of paramount importance for the duration of the resulting penicillinaemia that such PAM preparations should have certain minimum characteristics; for instance, diffusion from the intramuscular depot into the blood and tissues should take place with reasonable and defined slowness, notwithstanding the fact that individual variations have been observed in the rates of resorption and excretion through the kidneys. Certain minimum physical and other requirements which PAM preparations should meet have, therefore, been specified by the WHO Expert Committee on Venereal Infections and Treponematoses.[28] The desirability of following these international recommendations has been emphasized by the fact that several substandard PAM preparations have been found on the international market. These may result in inadequate treatment of patients and excessive relapse-rates.

Recently, new repository penicillin salts, such as *N.N'*dibenzylethylenediamine dipenicillin G and *N'*benzyl-β-phenylamine penicillin G, have been introduced which alone [29] or in combination with other penicillin salts [30] may give a penicillinaemia for several weeks with smaller doses than are necessary with PAM. Under WHO auspices these salts are at present under clinical trial in all the treponematoses in several parts of the world. These studies will supplement the relatively few data which have been published on this type of therapy and which have so far been confined to syphilis. A report on the first observations of the efficacy of *N.N'*dibenzylethylenediamine dipenicillin G in yaws is in preparation. Fig. 13 shows the duration of the penicillinaemia re-

[28] *Wld Hlth Org. techn. Rep. Ser.* 1953, **63**, 55

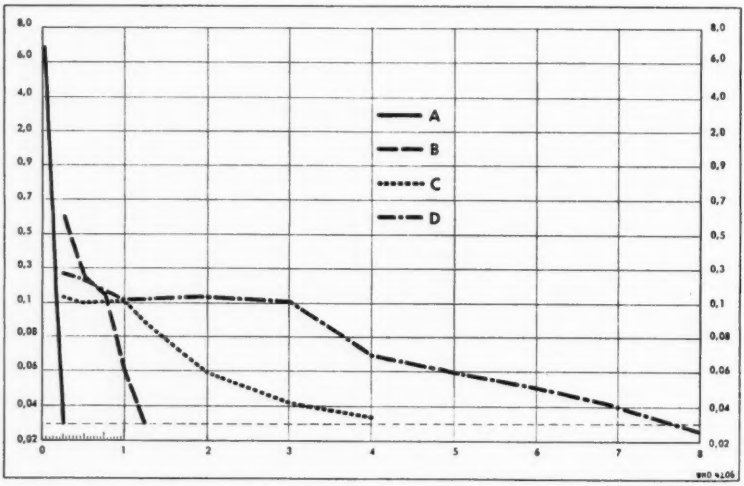
[29] Shafer, J. R. & Smith, C. A. (1954) *Bull. Wld Hlth Org.* (in press)

[30] Rein, C. R., Buckwalter, F. H., Mann, C. H., Landy, S. E. & Flax, S. (1953) *J. invest. Derm.* **21**, 435

sulting from intramuscular injections of various salts and preparations of penicillin.

In an appraisal of the value of penicillin in syphilis, Reynolds [31] stated, as early as 1946, that " penicillin is effective, but not always completely so. It is, in contrast to the metal chemotherapy, non-toxic, approaching the ideal in this respect. It is relatively easy to administer, and therapeutically effective amounts can be given in a comparatively brief period of time." Since then, experience with penicillin therapy in the other treponematoses as well has steadily grown ; and it may now be said that this statement requires only little modification to be applicable to them also. Indeed, it has become clear with the passage of time that therapeutically effective amounts can be administered in one or more repository intramuscular injections in a single session or, if convenient, in several sessions. On the other hand, evidence has accumulated that side-effects may result in a small proportion of cases in allergic patients or in persons sensitized by repeated previous use (or misuse) of small doses of penicillin. Considering that the consumption of penicillin has risen tremendously in all parts of the world in recent years, it is noteworthy both that no penicillin resistance has so far been reported in the treponemes and that side-effects are relatively infrequent and that their incidence is not increasing, being estimated by Kitchen et al.[32] at about 3%-5%. Isolated instances of death as a consequence of

FIG. 13. PENICILLINAEMIA RESULTING FROM INJECTION OF VARIOUS PENICILLIN PREPARATIONS



Test dose : 300,000 units, given intramuscularly

Abscissae : penicillinaemia, duration in days

Ordinates : penicillin, units/ml of serum

A — Crystalline penicillin G, aqueous solution

B — Procaine penicillin G, aqueous suspension

C — PAM (Procaine penicillin G with aluminium monostearate)

D — DBED (N.N' dibenzylethylenediamine dipenicillin G)

[31] Reynolds, F. W. (1946) *Amer. J. Med.* 1, 661

[32] Kitchen, D. K., Rein, C. R., Thomas, E. W. & Spoor, H. J. (1951) *Amer. J. Syph.* 35, 578

anaphylactic shock in allergic individuals have been reported.[33]

From the point of view of the patient, the physician, and the dispensary, and from that of health insurance systems and health administrations responsible for clinic programmes and mass treatment campaigns, it is essential that the treatment, besides being without frequent serious side-effects, be effective, inexpensive, and capable of being completed within a short time. An assessment of these four factors in different types of therapy in secondary syphilis is given in table IV, page 60.

The practical advantages of PAM brought out in table IV are undoubtedly responsible for the fact that this is at present the preparation of choice in the treatment of syphilis and the other treponematoses. This was confirmed by a recent worldwide survey, made by WHO, which showed that more than 80% of 277 leading venereologists and clinics relied on PAM alone in treating early syphilis, and by the technical discussions at the Sixth World Health Assembly, where PAM for treponematoses control was considered the drug which provided the maximum effect for the minimum expenditure.[34]

The medical world requires time and experience to clarify the details of dosage and administration of any new drug, and PAM in the treponematoses is no exception. It has been demonstrated in the last few years that a progressive doubling of the dosage of PAM—and consequently of the cost—does not correspondingly prolong the penicillinaemia. On the other hand, the amount of penicillin required in any particular case increases with the number of treponemes present; and, while only 300,000 units of PAM may be needed to cure most cases of early, primary, seronegative syphilis, this amount may cure only some 50%-60% of patients in the fully developed secondary stage, in which larger amounts of PAM are required to obtain a higher proportion of cures. In individual clinical programmes of the "urban demonstration and training project" type, fullest advantage should be taken of the properties of PAM, using amounts of at least 2.4 to 4.8 mega units in the early stages of syphilis. In selective public-health programmes against the treponematoses, considerations of administration and expense must, however, be taken into account when large numbers of infected persons are involved, as in mass treatment campaigns; and operational research in pilot areas has shown that as low a dosage as is compatible with reasonable clinical efficacy can be given in one or a few sessions. Good results for the majority must of necessity be preferred to perfection for the few. It is this "calculated risk" approach which has made it possible for health administrations, with the assistance of international organizations, to finance and undertake large mass campaigns against the treponematoses. A minimum dosage of 1.2 mega units of PAM is recommended for adults by the WHO Expert Committee on Venereal Infections and Treponematoses for the treatment of the endemic treponematoses; for venereal syphilis, 2.4 mega units are recommended for primary, and 4.8 mega units for secondary syphilis.

The availability of penicillin is thus the key to treponematosis control, as was pointed out several years ago by the WHO Expert Committee on Venereal Infections.[35] In the early days of its use, it was available only at a high cost to the privileged few, and many other diseases which were more immediately fatal had first call on the supply. Today it is produced in impressive quantities, and the total world production in 1953 probably exceeded 500 tons, corresponding to 300,000,000

[33] Welch, H., Lewis, C. N., Kerland, I. & Putnam, L. E. (1953) *Antibiot. and Chemother.* 3, 891

[34] *Chron. Wld Hlth Org.* 1953, 7, 205

[35] *Off. Rec. Wld Hlth Org.* 1949, 15, 20

TABLE IV. COMPARISON OF DIFFERENT TREATMENT METHODS IN SECONDARY SYPHILIS *

Assessment factor	Ideal therapy	Metal chemotherapy		Combined therapy		Penicillin alone	
		Neoarsphenamine and bismuth : four 3-month courses of 10 injections each	Arsenoxide : 1,200 mg by intravenous drip over 5 days	Amorphous aqueous penicillin : 5 mega units ; arsenoxide : 360-450 mg ; bismuth : 6-12 injections	Penicillin in oil-beeswax or with aluminium monostearate : 4.8 mega units ; bismuth : 10 injections	Procaine penicillin G with aluminium monostearate : 4.8 mega units	*N.N'* dibenzylethylene-diamine dipenicillin G 2.5 mega units
Therapeutic efficacy [1]	100	91.5	90.0	91.8 [6]	86.4	91.3	94.0 [7]
Toxicity : by-reactions [2]	0	9.5	8.5	3	0.91	0.12	0.3
mortality [3]	0	0.033	0.5	not reported	not reported	not reported	not reported
Convenience of administration [4]	100	50+ (ambulant)	90 (hospitalized)	65 (hospitalized and ambulant)	75+ (ambulant)	95-100 (ambulant)	95-100 (ambulant)
Drug cost [5]	—	92/8	190	—	10/4	9/9	10/8-12/6

* Based on data from the US Public Health Service, the British Clinical Co-operative Group, and the University Dermatological Clinic, Oslo

[1] Percentage of apparent cures at 24 months if the full course is given, and adjusted for estimated reinfections in the case of penicillin schedules with no adjuvant therapy

[2] Percentage of serious by-reactions

[3] Percentage of deaths due to treatment

[4] Percentage of patients completing prescribed course of therapy

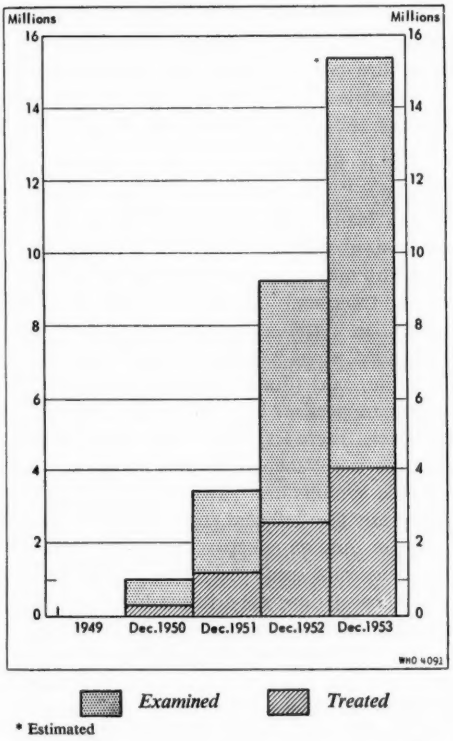
[5] Drug cost to clinics in Great Britain in shillings and pence at 1953 prices

[6] Includes seronegative and seropositive early syphilis

[7] 21 months' follow-up

mega units of penicillin, of which the USA produced some 70%. Penicillin is therefore now more readily available for general use; and, with international assistance, its beneficial effect in treating the treponematoses has been brought to millions of people (fig. 14). Further production is planned or

FIG. 14. NUMBER OF PERSONS PROTECTED AGAINST TREPONEMAL DISEASES IN MASS CAMPAIGNS 1948-53



* Estimated

under way in many areas of the world—sometimes with international assistance, as in India, Chile, and Yugoslavia—and it may be said that the world may now have enough penicillin to meet its immediate needs; but the demands of many countries are still below the level of medical necessity. An essential part of international aid to health administrations has thus been the supplying of penicillin for demonstration and training projects and for the first years of the mass treponematosis-control campaigns in underdeveloped areas.

MASS TREATMENT CAMPAIGNS

Since yaws and other endemic non-venereal treponematoses are found in rural and underdeveloped areas where medical facilities are absent or minimal, their control requires a communitywide rather than an individual approach, aimed at reducing the reservoir of infection as rapidly as possible to a level with which existing health facilities in the area can cope. Treponematosis-control efforts in such areas have been based on a wide application of penicillin by the entirely new public-health technique of mass treatment campaigns. Since there is no immunization against the treponematoses and no intermediate host to attack, and since facilities in rural areas are scarce, this approach is the only possible one.

Stages of a Campaign

Mass treatment campaigns are developed in five main stages,[36] the importance of each being determined by local conditions. These stages are :

(*a*) general preliminary analysis of the problem; (*b*) development of plans of operation; (*c*) demonstration, training, and survey phase; (*d*) expansion phase—the mass campaign proper—and (*e*) consolidation of the programme, including its integration into the strengthened local health services.

An important factor in any mass treatment campaign is the initial establishment of a pilot or control area in which selected groups may be examined, treated, and followed up by the different methods under investi-

[36] Reynolds, F. W., Guthe, T. & Samame, G. (1951) *J. vener. Dis. Inform.* 32, 263

gation and where full facilities are available for proper serological and other tests, for the recording of results, and for epidemiological evaluation. The experience gained from such operational research in the pilot or control areas may then be applied in a more general fashion to the campaign area as a whole, and the principles established there put into practice in projects elsewhere. At the outset, little experience was available on how to conduct mass campaigns; but now, as a result of work done by health administrations and WHO, experience is steadily mounting; and there can be little doubt that the investments in such operational research will pay practical and scientific dividends as the wider programme develops, a point which will be discussed later (see page 96).

Conduct of a Campaign

Several important lessons have been learned from the mass campaigns which have been carried out in recent years :

1. It is desirable in a mass campaign to examine the entire population. If this is not done, some infectious cases will be missed and the campaign may fail. Experience in Haiti has shown that the entire population cannot be examined by setting up permanent clinics and relying on the voluntary attendance of the patient. Even with suitable propaganda, less than 50% of the population may be reached. If mobile clinics are also provided in strategic areas, this figure may increase to 70%; and, if a house-to-house survey is made, the percentage will be 90 or more. It is now appreciated that a house-to-house technique is the best method of case-finding for most mass treatment campaigns.

2. It is necessary to revisit an area after mass treatment. It is evident that follow-up examinations are essential in order to deal with cases missed at the first examination owing to default or because they were in the incubation period at the time, with patients who have relapsed, or with persons who have recently migrated into the area. At these resurveys it is necessary to examine the entire population again. Experience in Indonesia and elsewhere has indicated that most of the infectious cases discovered in the villages that were re-examined would have been missed if the group originally treated had been the only one studied. It is considered, therefore, that, in order to obtain a lasting effect in mass campaigns against yaws, the entire population should be resurveyed at intervals of approximately one year in areas of initial high prevalence of infection.

3. It is necessary to give preventive or " abortive " treatment to contacts. Experience in Haiti, Thailand, and Yugoslavia has emphasized the importance of treating contacts who may have no overt signs of disease. In the treatment of venereal syphilis, this matter is still controversial, although Alexander et al.[37] have demonstrated that penicillin can afford almost complete protection to persons exposed to the infection. However, there is no doubt that in the endemic non-venereal treponematoses, e.g., endemic syphilis and yaws, the treatment of apparently non-infected contacts with penicillin is not only an effective, but also an essential, epidemiological procedure. Without it, control campaigns may, in the long run, fail, not only because persons in the incubation period will later develop the disease, but also because latent cases, which remain undetected when no serum tests are made, may relapse. " Contacts " have been differently defined in different campaigns, according to the prevalence of the disease and to environmental conditions. In some cases, a limited definition has been used, the term including only members of infected households; in other

[37] Alexander, L. J., Schoch, A. G. & Mantooth, W. B. (1949) *Amer. J. Syph.* 33, 429

cases, all children at risk under 15 years of age are included; and, in areas of very high prevalence, all community members may be considered to be at risk and treated as contacts.

Much experience has been gained in these campaigns and has been detailed in various technical publications by investigators of many nationalities. It is not intended to elaborate on this experience further in the present review of WHO activities on treponematoses control. However, consideration will be given later to some of the problems encountered in the expansion phase of the mass campaign, to the consolidation of the initial " knock-down " effect achieved by mass application of penicillin early in control programmes, and to the integration of the treponematosis-control programme into the general health services of the area.

Cost of Campaigns

The larger part of campaign costs are borne by the governments which are responsible for the projects. The costs are naturally higher in the earlier stages of the campaigns, since the initial investment in equipment, training of personnel, and organization is considerable.

It has already been pointed out (page 60) that the drug cost per patient completing treatment is now lower with penicillin than with metal chemotherapy. Early in the yaws campaigns, penicillin was more expensive than it is now, and the total average cost per person examined and treated in mass campaigns has, for this reason also, decreased since the inception of the campaigns.[38] Nevertheless, the cost of penicillin represents approximately half the expenditure per person treated in mass campaigns. The remaining costs concern project personnel, maintenance of transport and non-consumable equipment, replacement of consumable supplies, and hundreds of items relating to central and field administration.

In order to show the total costs and the cost per person examined and treated, including national and international commitments, these items are illustrated for three major mass campaigns in table V. The costs per person examined and per person treated have been calculated as averages from the beginning of each campaign up to, and including, December 1952; as has been indicated above, these costs decrease as the campaigns develop. For the period ending 1952, the cost per person treated ranged from $2.33 to $4.00 and, per person examined, from $0.39 to $0.43. Operational research in pilot and control areas showed that a single injection of a smaller dose of penicillin could replace the technique and

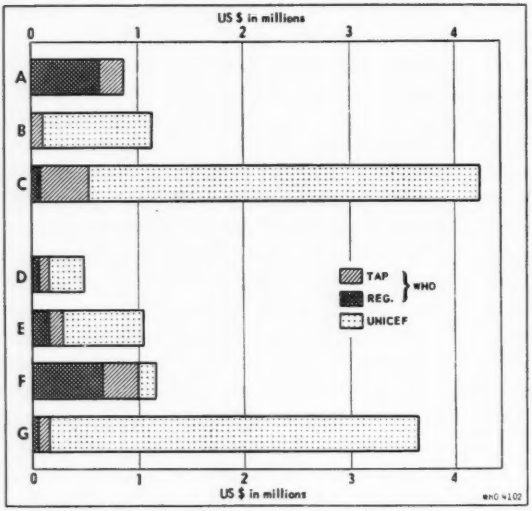
[38] Keeny, S. (1953) *Bull. Wld Hlth Org.* 8, 379

TABLE V. DISTRIBUTION OF COSTS, AND COST PER PERSON EXAMINED AND TREATED, IN THREE WHO/UNICEF-AIDED TREPONEMAL-DISEASE-CONTROL CAMPAIGNS *

Programme area	Contribution (US. $)					Cost per person examined (US. $)	Cost per person treated (US. $)
	Government	UNICEF	WHO	total	Government as percentage of total		
Philippines .	76,122	24,884	**	101,006	75.4	**	4.01
Thailand . .	369,832	259,511	33,534	662,877	53.8	0.43	2.76
Indonesia . .	718,310	855,200	19,317	1,592,827	45.1	0.39	2.33
Total . .	*1,164,264*	*1,139,595*	*52,851*	*2,356,710*	*49.4*	*0.41*	*3.30*

* From beginning of campaigns to end of 1952 ** Information not available

FIG. 15. NATIONAL AND INTERNATIONAL FUNDS FOR TREPONEMATOSIS CONTROL, 1949-53



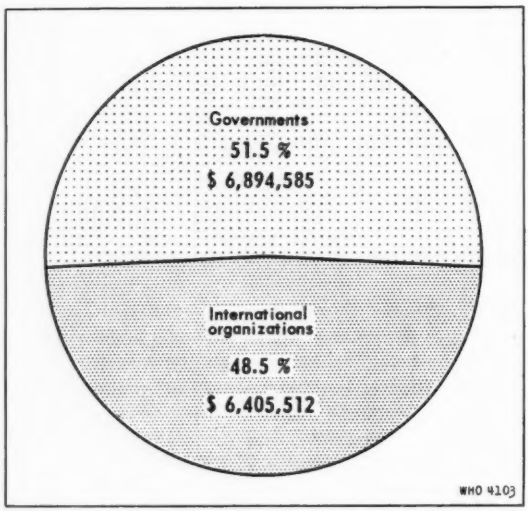
A — Demonstration projects
B — Maternal and child health/venereal disease projects
C — Mass campaigns

International expenditure by type of project and source of funds

D — Transport
E — Laboratory equipment and supplies
F — Personnel
G — Penicillin

International expenditure by category of expense and source of funds

TAP = Technical Assistance Programme
REG = Regular Budget

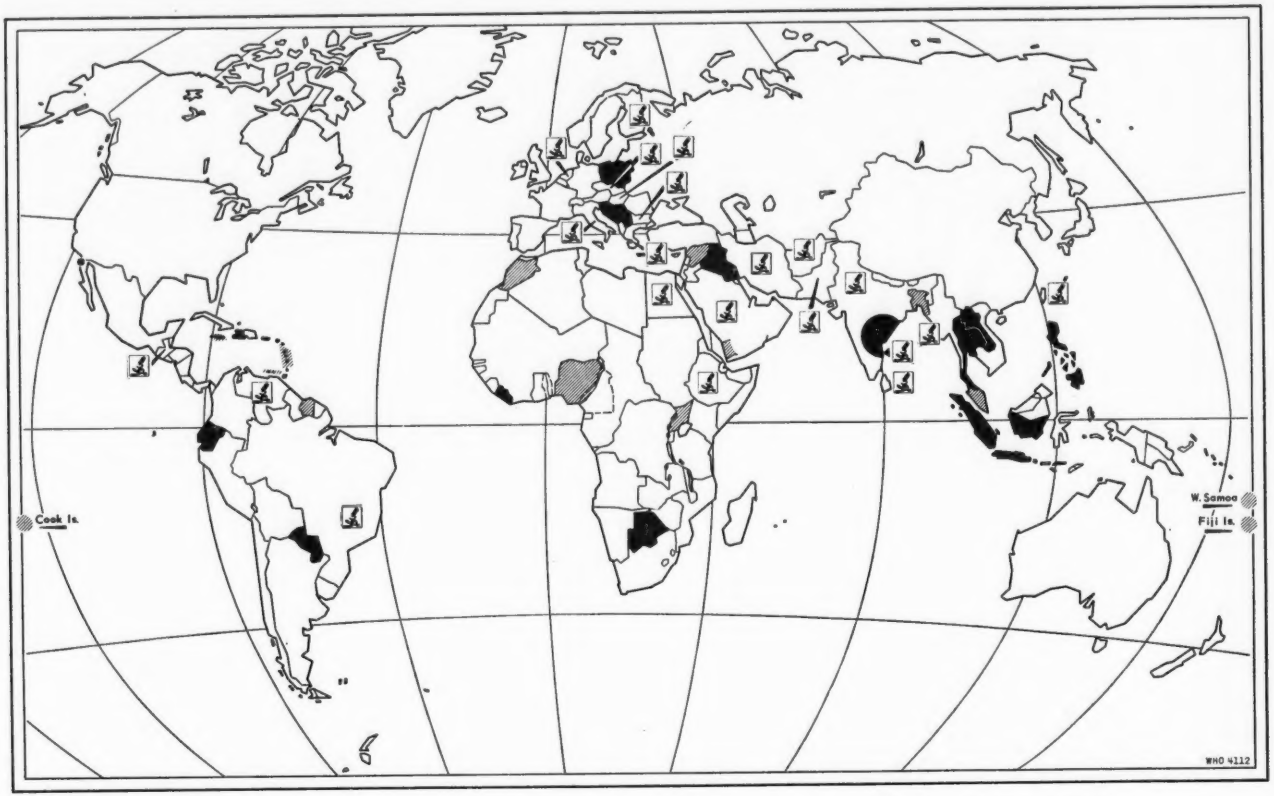


National expenditure: average percentage in four major campaigns used as basis for calculation of national expenditure in total programme

dosage initially used in several of the mass campaigns, provided that the PAM met WHO specifications. A saving of 34% in the expenditure for penicillin was thus effected, and operational costs were also reduced by the simplification of campaign procedures. The cumulative effect of this and the other factors already pointed out above has permitted the forecast that the cost per person examined and per person treated in such campaigns will drop to $0.10 and $1.00, respectively, in 1954.

Information concerning the costs of campaigns other than the three listed in this table is, thus far, less precise. However, the significant long-range commitments of health administrations in treponematosis control may, in general, be illustrated by fig. 15, which shows national and international funds expended, or allocated, during the five-year period 1949-53. It will be noted that the information is given by type of project and category of expense for mass campaigns, for demonstration and training projects, and for projects with emphasis on the control of prenatal and infantile syphilis, all of which are discussed in the following section.

FIG. 16. NATIONAL TREPONEMATOSIS-CONTROL PROJECTS, INTERNATIONALLY AIDED, UNDERTAKEN 1948-53, OR PROJECTED 1954-55



NATIONAL AND INTERNATIONAL ACTIVITIES IN TREPONEMATOSIS CONTROL

Since the Second World War, a number of governments in various parts of the world have wished to take advantage of, and to participate in, international co-operation for the control of the treponematoses. This international co-operation has taken several forms.

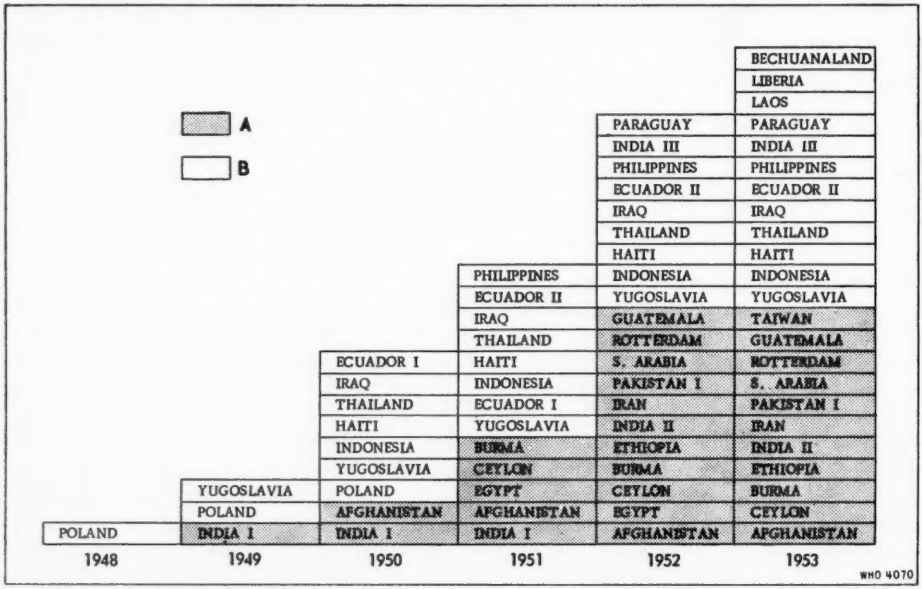
First, many health administrations which have attacked the treponematoses problem with new control methods, based principally on case-finding and on penicillin treatment of cases and contacts, have found it desirable to draw upon the experience and advice of health workers in other countries through the medium of WHO, and upon the co-ordinated assistance of WHO and UNICEF in providing supplies and equipment not locally available (e.g., Indonesia, Haiti, Thailand). The technical aid of WHO, under its regular budget or under the United Nations Technical Assistance programme, is frequently given to develop mass treatment campaigns, described previously as a new public-health technique in the control of the treponematoses.

A second type of activity has been the establishment or strengthening of demonstration and training projects. This has, in the past, proved a useful form of international health aid; and some countries (e.g., Ceylon, Egypt, India) have developed projects based on this approach. A well-equipped venereal-disease centre is established as a model for others to be set up later in different areas by local health administrations, and to serve as a training base for medical and auxiliary personnel. Such a centre, or clinic, is usually directed and operated by national staff assisted by an international team of advisers, which may include a venereologist, a serologist, a public-health nurse, and, sometimes, a health education specialist. In addition to diagnosis and treatment, the activities comprise epidemiological measures, including case-finding through home-visiting. Serological services not only are used for diagnosis and follow-up of cases treated in the centres, but also are applied to special, wider samples in different population-groups and in other parts of the country as the project develops. The demonstration and training centre is usually in an urban area and is, in a way, supplementary to the mass treatment campaign justified in rural areas, in which facilities are mobile and activities simplified because of the prevalence of the treponematoses and the more primitive conditions of health and environment in which it is carried out.

A third approach has been adopted in some countries with special problems of syphilis control : in these, as part of the general health programme, advantage has been taken of maternal and child health services in order to find cases of syphilis and to give treatment to children, adolescents, pregnant women, and nursing mothers. This approach was used in Finland and in some of the eastern European countries immediately after the Second World War. In other countries, such as Afghanistan, Burma, Pakistan, and Taiwan, venereal-disease control has been further emphasized in the maternal and child health programme by having a special section on venereal-disease control within the framework of the activities of the WHO advisory team.

The above aspects of treponematosis control call for special national efforts and long-term commitments under the communicable-disease-control programmes of the countries concerned. WHO's role is to meet the governments' requests for technical aid, through its machinery of regional offices, advisers, and consultants assigned to specific projects. In the five years from 1948 to 1953, WHO has assisted health administrations in many countries and in all regions in treponematosis control. Fig. 17 illustrates the expansion of the programme on a geographical basis for mass campaigns and for demonstration and training projects. The expanding nature of internationally aided programmes in terms of the increasing number of persons protected against the treponemal diseases in mass campaigns during the past several years has already been illustrated in fig. 14 (see page 61).

FIG. 17. TREPONEMATOSIS-CONTROL PROJECTS ASSISTED BY WHO AND UNICEF, 1948-53



A — Demonstration and training projects *B — Mass campaigns*

Roman numerals indicate more than one project in the same country.

In addition to aiding national efforts such as these, WHO has a more directly international function in co-ordinating and stimulating treponematosis control on an inter-country and inter-regional basis. As an international co-ordinator of health activities, WHO also grants fellowships; sponsors training courses; organizes seminars, symposia, and international conferences; encourages the exchange of scientific information; provides technical guidance through its expert committees; furthers the standardization of serological reagents and methods; co-ordinates special studies on particular treponematoses problems; and undertakes operational research aiming at the simplification of health techniques.

Finally, through collaboration with international non-governmental organizations interested in venereal disease and treponematosis control—such as the International Derma-

tological Congresses and the International Union against the Venereal Diseases—the programme of national health administrations and WHO may obtain support from voluntary organizations and professional societies in many countries. WHO maintains official relationships with the International Union against the Venereal Diseases, and various joint projects have been undertaken, such as the publication of information on national venereal-disease legislation throughout the world.

These various phases of the Organization's work will be considered in the articles which follow, though it must be emphasized that only a general review can be given here and that this account does not claim to be a complete catalogue of national and international treponematosis-control activities. Further information concerning national projects and WHO's programme in treponematosis control may be found in the medical literature, including other WHO publications such as the *Bulletin of the World Health Organization*, the Monograph Series, the Technical Report Series, and the *Official Records of the World Health Organization*, including the Annual Reports of the Director-General.

WHO OBJECTIVES IN TREPONEMATOSIS CONTROL

1. To stimulate the development of intensive and comprehensive health projects so that the treponematoses can be eliminated as public-health problems, and by such projects to contribute to the strengthening of local and national health services;

2. To contribute to the establishment in Member States of a practical degree of control of venereal syphilis (and other venereal infections) and to the prevention of their spread between countries and within special population-groups;

3. To stimulate teaching and training activities, to promote studies and exchange of scientific information, and to foster simplification and standardization of health techniques through operational and laboratory research, in an effort to co-ordinate national and international treponematosis-control activities.

THE CONTROL OF VENEREAL SYPHILIS IN VARIOUS COUNTRIES

Eastern Europe

Aid from UNRRA was requested by several health administrations in eastern Europe after the Second World War. Some of these requests were for assistance in the control of venereal syphilis, which had become a serious health problem in many areas as a result of the war. With the cessation of UNRRA activities, this type of aid became the responsibility of WHO and UNICEF, which provided technical advisers and consultants and certain supplies and equipment to the Governments of Bulgaria, Czechoslovakia, Hungary, and Poland for syphilis control. In some of these countries emphasis was on the control of prenatal and infantile syphilis, but in Czechoslovakia and Poland the control measures were of wider scope.

One of the first treponematosis-control projects in which international assistance was sought was in Poland. The Polish health administration undertook a syphilis-control campaign in which penicillin was used for the first time on a mass scale.

In 1947, mobile units were established for case-finding by mass serological screening examinations and for the health education of the public. The entire population of the areas concerned was examined, and positive reactors were directed to the nearest health centre for confirmation of the diagnosis. From the start of the campaign until the end of August 1948, 1,540,000 persons were examined by the Chediak test, which was found the most practical for mass screening. Of the 1,200,000 persons examined during 1948 alone, 21,772 had positive or doubtful serological findings; of these, 11,066 were confirmed by further examination.

Patients with early syphilis received 3-4.2 mega units of penicillin in oil-beeswax (POB) —the repository preparation available at that time. In the early stages of the campaign, this treatment was combined with a course of arsenoxide and bismuth. Pregnant women received 6 mega units of POB without adjuvant therapy, and children with congenital syphilis also received penicillin alone.

Four hundred and thirty-five physicians, 331 nurses, and 255 public-health nurses and social workers were recruited; training courses were open to all physicians in the country.

The Polish mass campaign was from the start integrated with the health services, which in effect were responsible for the organization of new treatment facilities; it also made use of the existing venereal-disease clinics, local health centres, and maternal and child health units.

Unfortunately, Poland has since 1950 ceased to be an active member of WHO, and precise information for evaluating the ultimate success of the campaign has therefore not become available to the Organization. The same is true of Bulgaria, Czechoslovakia, and Hungary, from which sufficient data have not been obtained to appraise the actual extent of the work and the results achieved.

Finland, Greece, Italy

The programmes in Finland, Greece, and Italy were designed to assist the Governments of these countries in the control of syphilis among pregnant women, nursing mothers, and infants. Equipment and supplies were

provided by UNICEF, and consultant services, medical literature, and fellowships by WHO.

In Finland, control of prenatal and infantile syphilis formed part of a nationwide venereal-disease-control campaign which, although well organized and operated, was restricted owing to economic and technical difficulties. International assistance enabled the Government to expand its efforts and to introduce modern methods of treatment and control on a wider scale. The proportion of pregnant women serologically examined for syphilis increased from 41% in 1946 to 92% in 1951, and the total number of blood specimens examined by the serological laboratories in the country increased from 288,885 in 1949 to 323,135 in 1950, an increase of about 12%. The great majority of syphilitic mothers were hospitalized before delivery for complete physical and serological examinations; post-natal examinations, including X-ray studies, of mothers and children were carried out at stated intervals. Although the specific death-rates attributed to syphilis have shown little change, a significant reduction took place in infant mortality due to syphilis in the period 1948-51. Despite the considerable decrease in the number of discovered cases of primary and secondary syphilis in the country as a whole, venereal-disease-control activities have not been relaxed; it would appear that, so long as these efforts continue, it is not likely that venereal disease will again be a public-health problem of great magnitude. This shows how appropriate aid to an already existing and effective venereal-disease-control programme can sustain and expand public-health activities.

In Greece and Italy, no nationwide venereal-disease campaigns were envisaged. After visits by WHO consultants, it was agreed that limited demonstrations of case-finding and of treating prenatal and infantile syphilis with penicillin should be undertaken.

In Italy, demonstration centres were established in Rome, Naples, Palermo, Messina, Catania, and Agrigento. In the centre at Naples, work began in 1948; but activities did not start in the other centres until the early autumn of 1949. By the end of 1950, 15,613 serological tests in prenatal syphilis had been carried out, and 1,074 in cases of infantile syphilis; 2,729 patients had been treated with penicillin, 2,181 of whom were pregnant women.

In 1950, the Italian Government distributed penicillin to all venereal-disease-control dispensaries in major towns in Italy.

In Greece, the Ministry of Health requested WHO/UNICEF assistance in 1949 to control syphilis among pregnant women in Athens, Piraeus, and Salonica. During 1950 and 1951, about 1,510 women and a similar number of congenitally syphilitic children were treated with penicillin. In 1950 a demonstration project for treatment of early syphilis in adults was established with WHO assistance in one of the major clinics in Athens.

India

A WHO venereal-disease demonstration team began work in the Himachal Pradesh in 1949 with the aim of developing venereal-disease control on modern lines at reasonable cost and of giving training in diagnosis, treatment, and control to local staff. Laboratory centres for bacteriological and serological procedures in the diagnosis of venereal disease were established, and stress was laid on the standardization of serodiagnostic techniques.

Treatment schedules were recommended, suited to local conditions; and the importance of controlling early infection and of preventing congenital syphilis was emphasized. Due attention was also paid to the desirability of special research work, the compilation of statistical data, and the value

of epidemiological investigation and case-finding.

Training was given in three-month courses, and the most satisfactory teaching method was found in seminars; technical demonstrations were carried out in the clinic, the laboratory, and the field.

During the first year, serological surveys were made in many areas in different parts of India. Wide variations in seropositivity of from 5% to over 50% of the population groups examined were revealed.

A limited mass campaign was undertaken in the Ghund area, where the prevalence of syphilis was found to be extremely high and where environmental conditions were such that the project could be subjected to certain controls. Altogether, about 1,556 persons were tested by the Meinicke and VDRL slide-test techniques, and 590 persons (38%) were treated, in 1949, with 300,000 units of PAM each. A sample re-examination of 453 persons was made six months later, and of 177 after a year.

Experience in this small pilot project indicated that large groups of people could be assembled for examination and treatment under extremely difficult field conditions and that, if simple slide-tests were used, laboratory examinations also could be carried out in the field and the results of the serum tests obtained on the same day as the specimens were taken. The immediate results of treatment indicated a satisfactory initial decrease in the reservoir of infection, and the number of new cases fell significantly.[1] At the follow-up examinations, a considerable lowering in the serological titre was also noticed, and the re-treatment rate was about 20%. A resurvey, for epidemiological study, is planned for 1955.

A demonstration project in progress in southern India is concerned with the strengthening of the facilities for teaching and research at the Venereal Disease Department of the Madras Medical College. The clinic there is probably one of the largest in the world : total attendance in 1949 amounted to 69,939 men and 20,320 women and children, and, in 1950, to 66,082 men and 24,131 women and children. In both years the number of new cases exceeded 15,000.

WHO has supplied a consultant serologist and a public-health nurse, in addition to laboratory and teaching equipment; and a medical social worker has been provided by the United Nations. The Madras Government has, for its part, considerably increased its staff and provided equipment and supplies for the further strengthening of the medical centre.

A special laboratory established in the Madras General Hospital participated in the first all-Indian serological evaluation programme, sponsored by the Indian Council for Medical Research. Six national laboratories in different parts of India participated, and the Madras laboratory acted as reference centre. Inter-state evaluation of the tests performed by field laboratories was also organized.

Afghanistan

A venereal-disease clinic and laboratory, working in co-operation with maternal and child health services, was established in 1950 at Kabul. WHO has provided medical advisers and nursing consultants, and UNICEF has provided important supplies.

Between March 1952 and July 1953, seven medical officers and nine nurses were trained in the venereal-disease clinic; eight medical officers, 24 laboratory technicians and assistants, and four nurses were trained in the laboratory. Lecture courses have been given to the local midwifery school, to student nurses at the maternity hospital, and to

[1] Cutler, J. C., et al. (1952) *Bull. Wld Hlth Org.* 5, 377

medical personnel at the Kabul military establishment.

Numerous serological surveys have been undertaken, and treatment has been given to patients with positive reactions. Home-visiting and epidemiological case-finding have been encouraged. A total of 5,153 persons have been tested, and the seropositivity has varied from 31% among prisoners at Herat to 0.6% among schoolchildren in different areas.

The laboratory has gradually increased its activities from serological testing for syphilis only to include various laboratory examinations of a general character; in fact, it is currently functioning as an expanded public-health laboratory for maternal and child health and other purposes.

Ecuador

In Ecuador, a small-scale demonstration for controlling syphilis by mass PAM treatment has been in operation in the Portoviejo and Manta regions since 1950. Each of these regions has a population of 5,000-6,000 persons between the ages of 15 and 50 years.

All persons in this age-group, whether or not they were infected with syphilis, have been given two injections of 1.2 mega units of PAM each, at five days' interval, and a serological test has been made at the time of the first injection, the patient being informed of the results at the second injection. Treatment has been given in the central clinic, at community centres, and on a mobile basis by a house-to-house canvass. By this means, a mass treatment campaign and a serological survey have been conducted simultaneously.

By September 1952, VDRL and Kahn serological tests had been done on 4,762 persons in Portoviejo; 404 (8.5%) were positive to both tests. Up to March 1953, some 7,223 people had been serologically tested in the campaign in Manta. A third campaign was organized in Bahia in May 1953.

Egypt

With the help of WHO, a demonstration centre was established in 1950 at Tanta, between Cairo and Alexandria, with the objects of furthering training of medical and auxiliary personnel; of standardizing diagnostic and treatment procedures; of stimulating interest in the promotion of health education; of encouraging case-finding, epidemiological, and other public-health methods; of carrying out operational research; and, finally, of studying the importance of the venereal-disease problem in the country as a whole. It was found that the incidence of syphilis was not as high as had originally been estimated by the health administration. The seropositivity among different population-groups, totalling 29,704 persons, varied between 17.3% and 0.2%.

The demonstration centre was later transferred to Cairo, where the international staff (a venereologist, laboratory physician, public-health nurse, and a health educator) was able to enter into more direct contact with university clinics, and to create interest in health education. The demonstration team introduced and gained wide acceptance of the use of PAM in syphilotherapy in national clinics throughout the country; newer antigens and modern serological methods were also introduced. Training courses were organized by the Ministry of Health for doctors, nurses, and serologists. Mobile venereal-disease-control field units were established.

The WHO team left Egypt at the end of 1952. However, venereal-disease control is going forward and is being extended. Thus, a mass serological examination of the population of the Siwa oasis in western Egypt was recently made : patients and contacts were treated, and the epidemiological and socio-

logical aspects were studied. The population of this oasis is being re-examined after six to eight months. This is an example of the kind of continuity which WHO seeks to foster when its direct assistance has ceased.

Burma

A model venereal-disease clinic and laboratory has been in operation in Rangoon since 1951 with WHO and UNICEF assistance. The clinic works in co-operation with five local venereal-disease centres, and four venereal-disease centres in other areas of the country have been established as part of the project. There has also been close co-operation with maternal and child welfare centres throughout the country and with a special skin clinic for the treatment of leprosy.

Between September 1951 and December 1953, a total of 34,571 cases of syphilis were found among 118,446 patients seen at the main clinic and the outlying clinics, including those in Mandalay, Moulmein, and Pegu. A number of special serological surveys have been undertaken, in which 39,378 persons were tested. The seropositivity varied from 25.4% among Rangoon port workers to 2.4% among Rangoon students.

At the Rangoon centre, medical officers, nurses, inspectors, laboratory technicians, and social workers have been trained by the international staff, comprising a venereologist, a laboratory expert, and a public-health nurse. In addition, lectures and clinical demonstrations have been given to medical students, student nurses, health visitors, students in public-health nursing, midwives, and other medical or para-medical personnel.

Ceylon

In 1951 a venereal-disease-control project was begun by the health administration of Ceylon, with WHO providing the services of a venereologist and a public-health nurse. It has been estimated that venereal diseases affect more than 10% of the total island population.[2]

A model clinic was established in Colombo to start the control of venereal diseases in the city. Collaboration is maintained with other medical and public-health activities, such as maternal and child welfare clinics and blood-banks. Three local subsidiary clinics and four outstation clinics, run by medical officers trained at the main clinic, have been set up in different parts of Ceylon. Between March 1952 and November 1953, 4,013 cases of syphilis were diagnosed among 22,479 patients seen at the central and other clinics. Special serological surveys have been conducted on a total of 46,853 persons, who showed a seropositivity varying from 11.9% among workers in private tanneries to 0.5% among schoolboys.

Since June 1952, a number of medical officers have been trained at the clinic, and courses of lectures have been given to doctors, postgraduate and undergraduate medical students, sanitary inspectors, nurses, rural leaders, and teachers from the training school.

Ethiopia

On the basis of recommendations resulting from a WHO survey,[3] a central venereal-disease clinic and laboratory was established at Addis Ababa in 1952 with the dual function of training national staff and of carrying out mass serological tests and penicillin treatment. WHO has furnished a venereologist, a serologist, and a public-health nurse. Technicians and auxiliary workers have been trained and will be sent out into the field in secondary teams to carry out mass penicillin treatment under

[2] Chelvarajah, T. (1947) *Ceylon Hlth News*, 13, 1
[3] Guthe, T. (1949) *Bull. Wld Hlth Org.* 2, 85

central supervision. The WHO team also helps in work against leprosy.

Special epidemiological studies in certain population-groups are being carried out in Addis Ababa, where the laboratory is performing serological tests on selected groups. Serological surveys of 7,080 persons have been made, and variations in seropositivity of from 82% among prostitutes in Addis Ababa to 2.3% among schoolchildren have been found.

Paraguay

The objective of a campaign in Paraguay, which began in 1952 on a limited scale, was to determine the prevalence of syphilis in the urban and rural area of Asunción-Villarrica, where a seropositivity of about 20% had previously been found, and to reduce the incidence of syphilis by modern methods of venereal-disease control. By November 1953, 13,200 persons had been examined, and 1,822 (14%) had been treated with single doses of 1.2 mega units of PAM. This pilot project will serve as the basis for a nationwide attempt to control venereal diseases.

Iran

In Iran, WHO is assisting the Government in the establishment of a modern venereal-disease-control and laboratory centre at Teheran and in the expansion and improvement of facilities for venereal-disease control in the country as a whole.

A three months' training course for medical and auxiliary personnel from different provinces started in September 1953 and was attended by 14 doctors, 7 laboratory technicians, and 27 physician aids. The staff trained at the centre will assist the Government in the initiation of venereal-disease control in other cities and in rural areas of the country.

As in other projects of this nature, advice is being given by a WHO venereologist, serologist, and public-health nurse.

Pakistan

In West Pakistan, efforts are being made to extend the existing venereal-disease-control facilities in and around Karachi, making new methods of treatment available to the local population of that city and to national and foreign merchant seamen. A fine, modern, clinic centre has recently been opened which will also be used as a training centre for national technical and professional staff. A WHO venereologist, serologist, and public-health nurse have been attached to this centre.

Among 9,484 patients seen at the Karachi centre between May and December 1953, there were 809 cases of syphilis (8.5%).

As in all such operations, the project is the responsibility of the national Government, which will establish smaller venereal-disease-control units in other parts of the country. These centres will be run by persons trained at Karachi. It is expected that these activities will later be expanded; and a venereal-disease centre is planned for Chittagong, East Pakistan, in 1955.

Saudi Arabia

A venereal-disease demonstration has been in operation at Mecca since 1952, with the assistance of a WHO venereologist and a serologist. Serological surveys conducted on 10,273 persons have shown a variation in seropositivity of from 33.4% in the armed forces to 8% among schoolchildren.

The object of the work has been to set up a clinic and a laboratory from which an investigation into the epidemiology of syphilis and other venereal infections in different parts of the country may be conducted, and where technical staff may be trained. It has been found that syphilis in certain areas of Saudi Arabia is of the endemic type, similar to that found in Bosnia, Yugoslavia.

Taiwan

A demonstration project was initiated in Taiwan in 1953, with WHO and UNICEF assistance. This project seeks to provide venereal-disease-control services for all pregnant women and for children and, ultimately, to establish an islandwide venereal-disease-control programme, including a special port demonstration.

Surveys will be carried out in order to assess the extent of the problem in Taiwan; for example, a serological survey of 1,660 teachers is at present in progress. The existing laboratory services will be strengthened and laboratory techniques standardized. Local staff is being trained by a team of national and international advisers, and health education is being emphasized. The main demonstration centre is at the provincial hospital in Taipeh.

ENDEMIC SYPHILIS IN BOSNIA

There is historical evidence that syphilis was introduced into Bosnia by the Ottoman armies in the 18th century. By the end of the 19th century, the disease was already widespread both in Bosnia and in Herzegovina. Owing to unhygienic living conditions, low educational and economic standards, and certain social customs, such as the common use of drinking vessels, the disease became endemic.

Investigations undertaken in Bosnia during the years 1905-11 indicated a prevalence of 8.3%, and a study carried out between 1926 and 1933 gave a figure of 11.8%. Before 1948, attempts to control endemic syphilis with neoarsphenamines were unsuccessful. In that year, the Yugoslav health administration initiated a nationwide syphilis-control programme, paying special attention to endemic syphilis in Bosnia, and requested the assistance of WHO and UNICEF. The approach to the problem was governed by the realization that, if the campaign against endemic syphilis was to succeed fully, it must accompany measures to improve the standards of education and health in general.

In this campaign, a systematic serological screening was undertaken in which approximately 435,000 persons, or 95% of the total census population of the endemic areas, were examined. In all, more than a million examinations and re-examinations were made. By the end of 1952, 35,238 persons, 8.1% of the examined population, had been treated with penicillin.

The campaign, directed from a central headquarters in Sarajevo, was carried out by three field groups, each composed of several teams, in co-operation with the local health officers of the districts being covered. During the early days of the campaign, infectious cases were treated with PAM, adults receiving a total of 3.6-4.2 mega units, in six or seven injections, given daily or every other day. Later, the total dosage was given in a single injection, and no difference was observed in the results. Finally, single injections of 1.8 mega units were used in a number of areas.

Although at the beginning it was felt that the greatest danger to the success of the campaign was the risk of relapses, it soon became apparent that this was negligible in comparison to the reinfections that occurred and the reactivation of endemic foci from cases that were missed, absent, or in the incubation period at the time of the first survey. The need for resurveys in which the entire population was again examined became evident. The best results were obtained when

TABLE VI. ENDEMIC SYPHILIS: EARLY INFECTIOUS LESIONS AND SEROPOSITIVITY OBSERVED IN FOUR SURVEYS IN MNO* SAPNA, BOSNIA, 1949-52

Area	Mean population**	Early infectious lesions								Seropositivity							
		number of cases				% of mean population				number of cases				% of mean population			
		survey No.				survey No.				survey No.				survey No.			
		I	II	III	IV	I	II	III	IV	I	II	III	IV	I	II	III	IV
1. Kraljevići . .	418	30	1	1	0	7.2	0.2	0.2	0	130	64	8	3	31.1	15.3	1.9	0.7
2. Ramići . . .	313	29	7	5	0	9.3	2.2	1.6	0	103	57	17	5	32.9	18.2	5.4	1.6
3. Medjedja . .	356	24	4	3	0	6.7	1.1	0.8	0	212	116	97	8	59.6	32.6	27.2	2.2
4. Goduš . . .	354	16	1	2	0	4.5	0.3	0.6	0	70	46	14	3	19.8	13.0	4.0	0.8
5. Sapna . . .	495	10	0	7	0	2.0	0	1.4	0	85	41	24	10	17.2	8.3	4.8	2.0
6. Andjelići . .	273	7	0	0	0	2.6	0	0	0	78	26	5	3	28.6	9.5	1.8	1.1
7. Mahmutovići	225	7	0	0	0	3.1	0	0	0	44	18	1	1	19.6	8.0	0.4	0.4
8. Kovačevići .	307	7	4	4	0	2.3	1.3	1.3	0	54	31	7	2	17.6	10.1	2.3	0.7
9. M. Nezuk . .	416	5	0	0	0	1.2	0	0	0	97	57	15	12	23.3	13.7	3.6	2.9
10. Jusići . . .	195	1	0	0	0	0.5	0	0	0	23	12	3	0	11.8	6.2	1.5	0
Total	*3,352*	*136*	*17*	*22*	*0*	*4.1*	*0.5*	*0.7*	*0*	*896*	*468*	*191*	*47*	*26.7*	*14.0*	*5.7*	*1.4*

* " Mno " is a small administrative unit. The total area of Mno Sapna is 125 square kilometres (48 square miles).

** 94.5% of the mean total population was examined.

The four surveys were carried out on the following dates : I, 2 October 1949 ; II, 4 April 1950 ; III, 30 June 1951 ; IV, 10 January 1952. During each survey, the cases found were treated ; in survey III, household contacts were also treated.

the entire population was examined at the first survey and when treatment was given to all household and family contacts. The abortive treatment of such contacts consisted of single injections of 1.2 mega units of PAM.

The gradual decline in the numbers of early infectious cases and in seropositivity is well illustrated in table VI and fig. 18.

The valuable experience gained in this programme has been described by its director, Dr. E. I. Grin,[4] who points out :

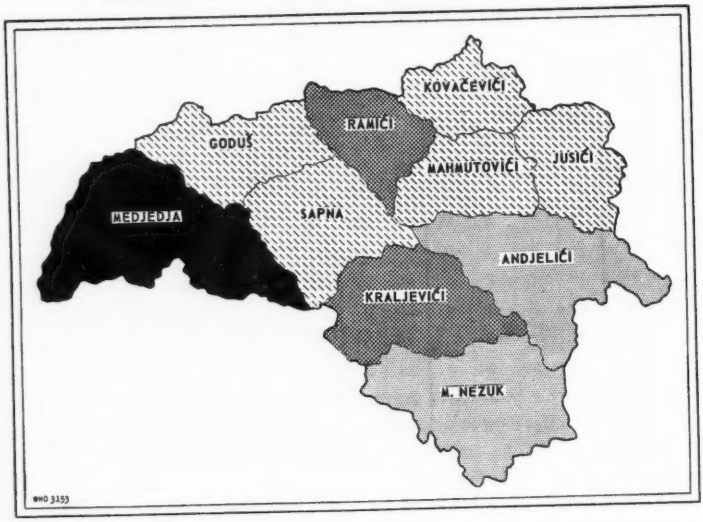
" The reservoir as a whole has been brought under control, and the attitude of the people to the problem has been altered; this is due partly to some general improvement in the social and economic conditions, partly to the work of the field teams and to the general progress of the campaign, and partly to the fact that new cases of endemic syphilis are now detected more rapidly and can be more quickly dealt with. . . .

" The epidemiological situation cannot conceivably return to its original form after one or two follow-up examinations have been made, but constant supervision of previously endemic areas is necessary as part of the long-term programme. In Bosnia, such supervision and health control are provided by one or more health workers' remaining in the field between control examinations and after the field campaign proper has come to an end. Being selected from the field teams, they are familiar with endemic syphilis as a rural health problem in all its aspects. . . . The health workers co-operate with the local health centres, which assume the responsibility for keeping the disease under control through their normal machinery against communicable diseases, in the ' consolidation phase ' of the long-term programme.

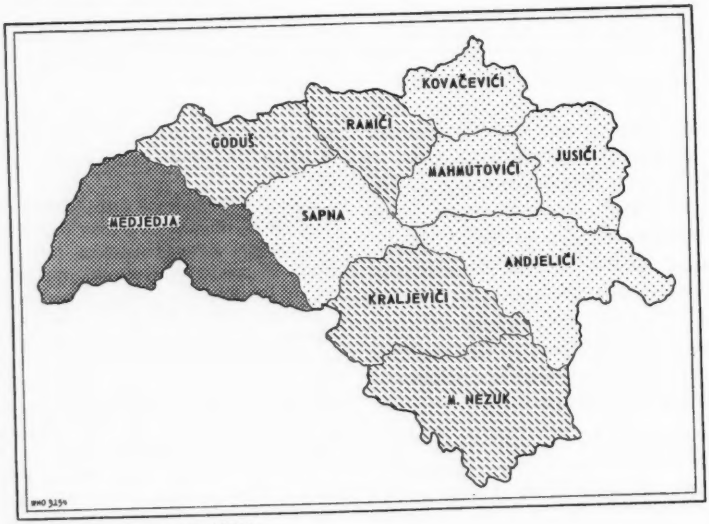
" The present programme is serving as a bridgehead to the development of general public-health services and to the expansion of the machinery against communicable diseases . . . "

[4] Grin, E. I. (1953) *Epidemiology and control of endemic syphilis : report on a mass-treatment campaign in Bosnia*, Geneva (*World Health Organization : Monograph Series* No. 11), pp. 75, 78

FIG. 18. DECREASING PERCENTAGE OF SEROREACTORS FOLLOWING MASS TREATMENT CAMPAIGN AGAINST ENDEMIC SYPHILIS IN BOSNIA *



First survey: October 1949

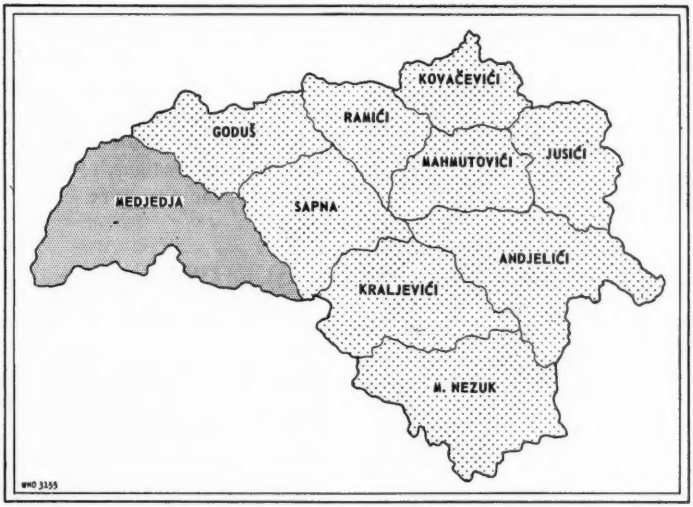


Second survey: April 1950

% Seroreactors

0.4–10.1 | 11.8–19.8 | 23.3–28.6 | 31.1–32.9 | 59.6

* *See table VI, page 77.*



Third survey : June 1951

Fourth survey : January 1952

% *Seroreactors*

0.4–10.1	23.3–28.6	59.6
11.8–19.8	31.1–32.9	

These are satisfactory conclusions, and they indicate :

(*a*) that a treponematosis can be brought under control by means of mass treatment with penicillin, if suitably applied;

(*b*) that a programme to combat endemic syphilis itself stimulates social advancement, which in turn renders the environment unsympathetic to the return of the disease; and

(*c*) that a treponematosis project can serve as a bridgehead for future public-health activity.

It is believed that the campaign in Bosnia not only is to the considerable credit of the local health administration, but also has been one in which most useful experience has been gained for application in the management of other mass campaigns, of which it has been, in its way, the prototype.

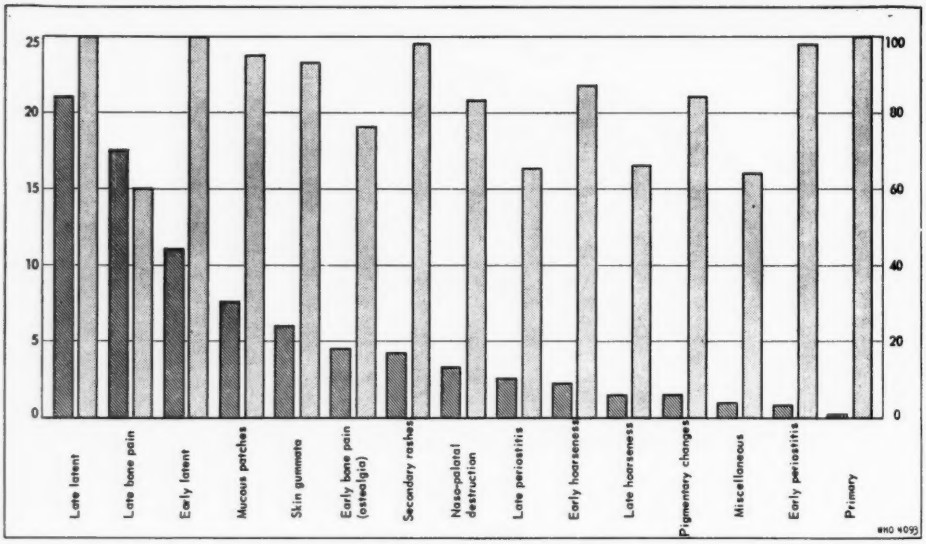
BEJEL AND DICHUCHWA

Bejel in Iraq

In Iraq, treponematosis-control activities are centred on bejel, the syphilis-like disease described by Hudson [5] in 1928. A joint WHO/UNICEF-aided demonstration in bejel control was initiated in 1950. An area in the Ramadi region, north of Baghdad, was first selected for study; later, surveys were undertaken in the Mosul region in the north, the Amara region in the south and, subsequently, in other areas. It became apparent that the disease was not so widespread as had first been feared and that it occurred most frequently in the river-bed areas and particu-

[5] Hudson, E. H. (1928) *Nav. med. Bull. (Wash.)*, **26**, 817

FIG. 19. PERCENTAGE DISTRIBUTION OF CLINICAL SYMPTOMS AND SEROPOSITIVITY IN BEJEL



Cross-section of 3,507 cases of untreated bejel

% of total patients with particular symptom (scale on left: clinical symptoms)

% seroreactors (scale on right: seroreactors)

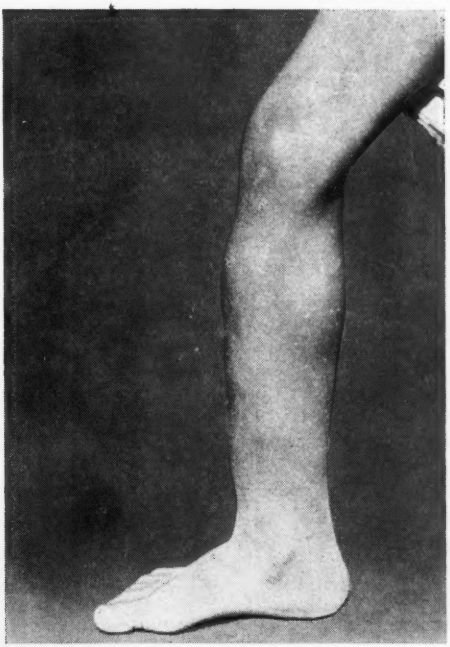
larly among the marsh Arabs of Amara, where the difficulties of transport were greatest and the people therefore most isolated.

The areas where bejel is prevalent have been the site of a mass campaign of treatment with penicillin. By the end of December 1953, more than 134,000 persons had been examined, and more than 78,000 cases and contacts treated. Progress in this campaign has been less rapid than in similar WHO/UNICEF-assisted projects, partly because the population is widely scattered and because the facilities for communication and transportation in the areas of high prevalence are limited.

FIG. 20. EARLY BEJEL

General papular eruption in woman three weeks pregnant. This patient was treated with 1.2 mega units of PAM and at term delivered a healthy, seronegative child. (G. Csonka, London)

FIG. 21. LATE BEJEL



In late stages of the treponematoses, there may be painful osteoperiostitis, as illustrated above in a case of bejel. (G. Csonka, London)

As has been indicated on page 50, there is great similarity in the epidemiology and in clinical manifestations of bejel and endemic syphilis. The late lesions are comparable to the gummata, osteoperiostitis, and nasal, laryngeal, and palatal lesions of benign tertiary syphilis. A cross-section of 3,507 cases of untreated bejel confirms this view [6] and is illustrated in fig. 19.

Bejel lesions, observed in Iraq, are shown in fig. 20 and 21. Other examples, including one of extreme mutilation, have been described by Jones.[7]

[6] Csonka, G. (1953) *Brit. J. vener. Dis.* **29**, 95
[7] Jones, L. G. G. (1953) *Brit. J. vener. Dis.* **29**, 104

FIG. 22. EFFECTIVENESS OF PENICILLIN IN BEJEL

Even in far-advanced, late cases of bejel, the infection may be arrested by a single injection of long-acting penicillin, as shown in the above photographs. Left, before treatment; right, three weeks after one injection of 2.4 mega units of PAM. (L. G. G. Jones, London)

Dichuchwa in Bechuanaland

It has already been mentioned that dichuchwa, a treponematosis similar to, or identical with, endemic syphilis and bejel is encountered in some parts of Africa. A joint WHO/UNICEF programme to control this infection was initiated in Bechuanaland in November 1953.

Field operations during the first year of the project are being limited to a study of the epidemiological, clinical, and serological aspects of the infection, including the response to treatment of cases and contacts. The Bakwena Reserve, which is occupied by the 40,000 members of the Bakwena tribe, has been selected for the preliminary investigations; control and follow-up measures are being undertaken on a family basis. Treatment is being given to all active cases of treponemal diseases, to all latent cases (as determined by anamnesis), and to the contacts of infectious cases. Contacts have been defined as all adults in the same house, and all children under the age of 16 years in the same kraal as any infectious case.

In November and December 1953, 5,000 persons were examined. Information obtained thus far will form the basis for a mass treatment campaign which will begin, with UNICEF assistance, towards the end of 1954.

MASS CAMPAIGNS AGAINST YAWS

Haiti

Of 3.5 million people living in the Republic of Haiti, approximately five out of six live in underdeveloped rural areas where yaws has for some time been rampant. Although it is difficult to estimate the prevalence of the disease in the past, it is thought that approximately 1.5 million people had yaws a few years ago.

In 1941, on the request of the Government of Haiti to the Pan American Sanitary Bureau, a yaws survey was made and plans put forward for the control of the disease. Early in 1942 a limited programme, based on treatment at stationary clinics, was started jointly by the Government of Haiti and the Institute of Inter-American Affairs. At first, metal chemotherapy was used, but later penicillin was substituted, after a demonstration of the excellent effects of penicillin in oil and beeswax.[8]

In 1948, the United Nations Mission of Technical Assistance to the Republic of Haiti recommended that an organized nationwide mass campaign with penicillin be undertaken. This proposal was considered by the WHO Expert Committee on Venereal Infections in 1949,[9] which recommended that in the Republic of Haiti and the Dominican Republic an epidemiological experiment be carried out, with simple mass techniques and using procaine penicillin in oil with aluminium monostearate (PAM).

The present campaign began in July 1950, with a team of WHO technical advisers and UNICEF supplies, and has been in continuous operation since that time. The simplest methods have been used throughout. As medical staff is limited, mass treatment has been carried out by rapidly trained auxiliary personnel; and local inspectors who are also qualified chauffeur-mechanics have performed the bulk of the work. These "injectors" have given treatment to everybody, regardless of age or clinical or anamnestic evidence of yaws. Satisfactory results have been obtained by giving 600,000 units of PAM to yaws cases; those without clinical manifestations or history of the disease have received only 300,000 units; and children and infants have been given proportionately smaller doses.

By the autumn of 1951, 666,738 persons had been treated in clinics. When the first census figures became available, however, it was found that an insufficient percentage of the population was being reached, and a change was made to a house-to-house method of treatment in which each person seen was given an injection of penicillin, in the same doses as before. With this method, 1,700,240 persons (about 97% of the population of the new areas covered) were treated between October 1951 and September 1953. Sample surveys carried out in these areas eight months after treatment showed that the initial "knock-down" had been satisfactory: very few cases of infectious yaws were found. On the other hand, in the areas that relied on the fixed clinic system, and where substandard penicillin had been used in some cases, isolated foci of infection persisted; and some of them had already begun to expand. It has therefore become necessary to revisit each house in these areas, treating all persons, regardless of presence or absence of the disease, with a satisfactory penicillin.

There is a substantial focus of venereal syphilis in the urban area in and around

[8] Dwinelle, J. H., Sheldon, A. J., Rein, C. R. & Sternberg, T. H. (1947) *Amer. J. trop. Med.* 27, 633

[9] *Wld Hlth Org. techn. Rep. Ser.* 1950, 13, 16

Port-au-Prince, and measures against it, before the Haiti programme is completed, are being considered.

Haiti is only one part of an island shared by the Dominican Republic. It is clear, therefore, that the eradication of yaws will be difficult unless control efforts are undertaken in the border areas of the Dominican Republic as well, and steps to this end are under consideration.

Indonesia

The population of Indonesia is estimated at 75 million, the vast majority living in rural areas. It has been stated that there are about 10 million cases of yaws in the country.

Active yaws work was carried out with arsenicals in Indonesia before the Second World War; but, during the war, control measures were discontinued, and a sharp rise in the incidence of the disease took place. Plans for the control of yaws, with the help of WHO and UNICEF, were drawn up by the Indonesian Government and WHO consultants, and the work began in May 1950. Starting with two areas in the residencies of Jakarta and Jogjakarta, the operations have since been extended to west Java, Bali and Flores, north Sumatra, and South and West Kalimantan (Borneo).

The campaign is based on teams of six or eight trained nurses working under the supervision of full-time and part-time medical officers. Owing to the shortage of personnel, a scheme has been introduced by which 200 assistant nurses working in dispensaries under the supervision of the trained nurses are being instructed in the diagnosis and treatment of yaws. Early in 1953 there were 24 regular mass treatment teams and 35 simplified teams in the field. These teams examine the entire populations of villages, and all patients with active yaws are asked to report to a site where the diagnosis is checked and treatment administered.

The campaign as a whole is run from headquarters at Jogjakarta, from which several important pilot studies have been carried out to determine the efficacy of various treatment schedules and methods of approach to the communities. A study is also being made of the efficacy of diamine penicillin under tropical conditions.

At the beginning of the campaign, adults were treated with two injections of 1.2 mega units of PAM each, given at intervals of from four to seven days; smaller doses were given to children. Recently, single injections of 1.8 mega units have been given. It is now accepted in principle that the treatment of apparently non-infected house and school contacts with half this dosage is necessary. To date, however, comparatively few contacts have been treated.

In all, a total of 6,745,515 persons had been examined and 1,079,224 treated up to the end of 1953. No fewer than 73,205 persons were treated for the first time during resurveys, indicating the necessity of re-examining the total population on these occasions. The populations covered have frequently reached the desired level of 90%.

Thailand

Of the 18.3 million people in Thailand, it is estimated that approximately 60%, or about 11 million, live in areas where yaws is found. From surveys of these areas, it is estimated that there may be about 1,430,000 cases of yaws. The distribution of the disease is patchy, but here as elsewhere it is associated with remoteness, filth, and low standards of personal hygiene. Previously, arsenicals were administered at a few stationary rural clinics; but, as in other parts of the world, they had little or no effect in controlling the disease.

A WHO/UNICEF-assisted campaign began in April 1950. The campaign is being carried out by mobile teams composed of one medical officer and usually four auxiliary workers; 17 regular teams and three follow-up teams are at present at work. A WHO team of advisers is assisting the national health administration.

Until the end of October 1952, the treatment consisted of two injections of 1.2 mega units of PAM each. Since that time, single injections of 1.2-1.8 mega units of PAM have been given. The Government has supplied one-third of the penicillin, and UNICEF, two-thirds.

Where the prevalence of yaws is 15% or over, or where there is a high proportion of infectious cases, the treatment of contacts has been extended to include not only household contacts, but also all contacts in the same class at school as children found to have infectious yaws. Resurveys are being undertaken in the treated areas.

In the three and a half years up to November 1953, a total of 2,581,879 persons had been examined (first examination); 317,892 had been treated for the first time, and 6,391, re-treated. About 34,093 of the treated cases were discovered at resurvey. It was planned that about 750,000 people were to be examined in the second half of 1953 and 1,750,000 in 1954. At the present rate of progress, the work will continue for the next three to five years. Approximately 54% of the cost is borne by the Government and 46% by UNICEF.

Philippines

The Philippine archipelago consists of 7,021 islands with a total population of about 20 million, of whom three-quarters live in rural areas. Yaws is reported to be endemic in 39 of the 51 provinces; in 30 of these the prevalence is reported to be less than 1%, but in the remaining nine the average prevalence is 3.6% and reaches 30% in certain areas. The disease is most common on the smaller islands, along the sea coast, along rivers, and in the swampy regions of the larger islands.

The Philippine Government, assisted by WHO and UNICEF, began a yaws-control campaign in April 1951 in the nine provinces with the highest prevalence. The campaign was started in the island provinces of Samar and Leyte, where the prevalence was believed to be about 8% among the rural population. There are altogether six mobile teams, which travel from village to village; the population is told in advance when the team will arrive, and a census is taken. Local sanitary inspectors and other health personnel work with the team and are given training in yaws control. As the teams move on, the records are left behind in the charge of the president of the sanitary division, who arranges for the follow-up of those treated. In this manner the campaign becomes integrated into the public-health structure of the province.

Treatment was originally given by injections of 0.6 mega units of PAM for children under ten years of age and two injections of 1.2 mega units each for adults. These doses were changed to accord with recommendations made at the First International Symposium on Yaws Control, which was held in Bangkok in 1952. A single-injection procedure is now being used. Up to December 1953, 1,880,867 persons had been examined and 71,783 treated with penicillin.

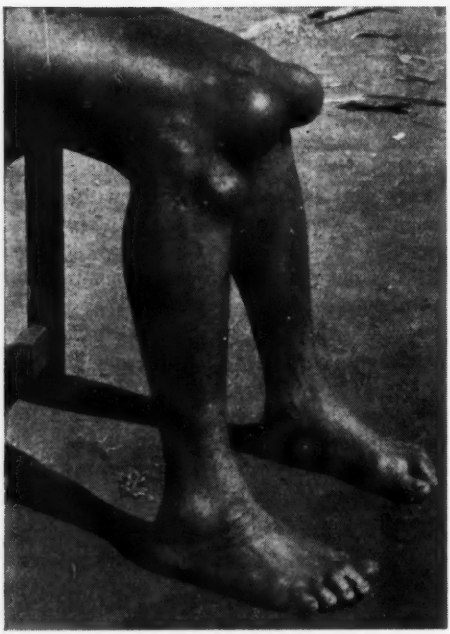
Resurveys of the control areas and of all areas in which the prevalence exceeded 10% have been carried out by two teams. The results of one resurvey showed a prevalence of 2.48% in a population of 16,000 persons, as compared with 18% at the first survey.

India

There are pockets of yaws in India in parts of the Madhya Pradesh and adjoining States.

FIG. 23. LESIONS OF YAWS

Indolent ulceration of the elbow (C. J. Hackett, London)



Juxta-articular nodules in patellar region
C. J. Hackett, London)

Bone deformation in tertiary yaws
(E. E. Kruizinga, Rijswijk, Netherlands)

Generalized, multiple papillomata
(F. N. Guimarães, Rio de Janeiro)

Gross gangosa (rhinopharyngitis mutilans)
(C. J. Hackett, London)

Incapacitating, plantar, hyper-keratotic lesions
(F. N. Guimarães, Rio de Janeiro)

An active campaign undertaken by the State Government of Madhya Pradesh in the years 1941-45 was successful in reducing the incidence of the disease, but financial stringency brought it to an end and the incidence has since increased.

A campaign to stamp out yaws from this area has now begun, with WHO and UNICEF assistance. It started as a pilot project in the Madhya Pradesh and was extended to the State of Hyderabad in July 1953; it is proposed to extend it later to the other adjoining States. Up to November 1953, 85% of the total population of 79,813 persons in 556 villages had been examined; 3,789 cases of yaws (5.6%) had been found, and persons with lesions or a history of yaws and contacts of infectious cases had been treated.

Laos

The population of Laos is estimated at 1.5 million; in the four southern provinces, with a population of 610,000, the estimated prevalence of yaws in some areas is between 10% and 15%. Conditions of security and communications allow approximately 60% of the population in the south to be reached by jeep, but only in the dry season.

Previously, yaws cases were treated with arsenicals at stationary clinics; but a project for survey, training, and mass treatment is now under way, conducted with international assistance by one mobile team. Since April 1953, 97,212 persons have been examined and 5,821 persons, including 829 contacts, treated with penicillin.

Liberia

In Liberia, where the population is about 1.5 million, malaria and yaws are the main public-health problems. It is estimated that approximately 30% of the population are afflicted with yaws. Even in the capital, Monrovia, there is a reported prevalence of 16% to 19%.

With international assistance, a survey of a population of 50,000 was begun in March 1953 in the vicinity of Ganta, where malaria is also very prevalent. A house-to-house survey of the Kpaing area began in August 1953, and resurveys will take place at intervals of six months. These surveys will be combined with antimalaria activities. All clinical cases found will be treated with penicillin, and contacts will receive preventive doses. In the Bahn area, field surveys have so far been undertaken in 16 villages, where 4,918 persons have been examined, of whom 63.9% were found to have yaws.

Up to December 1953, 14,846 persons had been examined and 10,840 treated (including contacts) in this project.

SYPHILIS CONTROL IN SPECIAL POPULATION-GROUPS

Certain population-groups require consideration as units, although their individual members may come from many countries. Among such groups are refugees, migrants, and seafarers.

Refugees

The problem of refugees was at its height immediately after the Second World War. The need for controlling venereal diseases, particularly syphilis, in vast groups in Europe and Asia was recognized at the time; and the importance of reducing congenital syphilis was included in the plans for the maternal and child health activities of the international organizations. Work to this end was undertaken in Europe first by UNRRA and later by the former Inter-

national Refugee Organization (IRO) and WHO.

Refugees still present a problem in many parts of the world. More than 850,000 Arabs have been living for some years in camps in Lebanon, Syria, the Hashemite Kingdom of the Jordan, and the Gaza area of Israel. As part of the international aid which they receive, considerable attention is paid to the improvement of maternal and child health and to the control of communicable diseases, including syphilis.

A serological survey carried out in 1950-51 among 8,259 pregnant women in Lebanon, Syria, and Gaza showed that 5.3% of them were serologically positive for syphilis. WHO arranged for these women to be treated with penicillin and undertook the necessary measures for the general control of syphilis. At the same time, the Organization took steps to ensure that the laboratory procedures used in the diagnosis of cases were of the highest standard.

Other refugees—for example, those displaced by the partition of India and lodged in camps in Pakistan—have been assisted through demonstration centres established with international assistance.

Migrants

Consultations have taken place between the International Labour Organisation (ILO), IRO, and WHO on the medical requirements of various countries which have been or are accepting immigrants, and on the requirements as to persons who have been treated for syphilis. Countries that accept immigrant labour have different medical requirements, and it is desirable to ensure that persons emigrating from one country to another are not turned back on arrival because of those differences.

In the days before penicillin, persons with positive serological tests for syphilis (excluding those with biological false-positive reactions) were often considered ineligible as immigrants. However, new and effective methods of treatment with penicillin, and the realization that a positive serological test does not always mean active syphilis in adequately treated persons with a negative spinal fluid, have led several nations to change their regulations. This change, fostered in part by WHO, has brought hope to thousands of persons in desperate situations who were hitherto automatically precluded from emigration to new countries.

Seafarers

The historical importance of seafarers in the dissemination of syphilis has been appreciated since the time of the classical epidemic of syphilis which spread through Europe after the return of Columbus from the New World. The development of the steamship in the 19th century and the realization of its potential in the 20th century gave rise to much concern about the spread of venereal diseases by seafarers. This resulted in the Brussels Agreement of 1924, which provided for free treatment in the major ports for seafarers suffering from venereal infections. Fifty-seven countries and their overseas territories have adhered to this Agreement, which was established on the initiative of the Red Cross, the International Union against Venereal Diseases, and the International Labour Organisation. WHO took over the administration of the Agreement from the Office International d'Hygiène Publique in 1948.

Because of the striking changes in the nature and extent of the treatment of syphilis and other venereal infections, WHO, on the recommendation of the First Health Assembly,[10] assumed the responsibility for studying the possibility of revising the Brussels Agreement, with a view to establishing WHO

[10] *Off. Rec. Wld Hlth Org.* 1948, 13, 303

health regulations in this field similar in principle to those for quarantinable or pestilential diseases. No definite steps were taken until the pattern of the new international regulations with regard to other diseases should become clear with the coming into force of the International Sanitary Regulations in 1952. In the meantime, on the suggestion of the International Union against Venereal Diseases, the Netherlands Government established the Rotterdam Port Demonstration Centre, with the assistance of WHO. Among the activities of the Centre is the study of certain aspects of maritime venereal-disease control and of the functioning of the Brussels Agreement.

The control of venereal disease among seafarers, and the place of venereal infections in maritime public health in general, were also considered by the Joint ILO/WHO Committee on the Hygiene of Seafarers in 1949,[11] and will be studied again when this committee meets in April 1954. It is expected that the legal aspects of the Brussels Agreement will be considered by WHO in 1955, and that a study of the proposed WHO health regulations will subsequently be transmitted to governments and to the interested international organizations.

WHO has published a revised edition of the *International list of venereal-disease treatment centres at ports*, which gives venereal-disease clinics in the major ports throughout the world and the hours of attendance. A further edition is due in 1955. Similarly, the individual treatment record booklet issued under the Brussels Agreement has been revised and brought up to date.

In its role as administrator of the Agreement, WHO receives complaints from health administrations about services in ports and acts as intermediary between the governments concerned. The exchange of epidemiological information is also encouraged.

WHO was instrumental, through its headquarters and its Regional Office for Europe, in the establishment of the International Anti-Venereal-Disease Commission of the Rhine, an intergovernmental body on which were represented the five countries sharing the Rhine River system.

Finally, WHO sometimes assists governments directly in the establishment of port treatment facilities for venereal infections, e.g., in Karachi, Pakistan.

The technical interest of WHO in maritime venereal-disease control has been in fostering standardized methods of diagnosis and therapy among seafarers so as to obtain more uniform treatment schedules and serological tests at ports in different countries. Although wide variations still exist, the introduction of penicillin therapy in syphilis has greatly simplified the previously complicated situation resulting from the need to retain seafarers for prolonged treatment ashore with metal chemotherapy. The facts that penicillin treatment of early syphilis requires only a few sessions and that the patient need not be hospitalized have substantially reduced absenteeism and the number of man-days lost in home and foreign ports, which is an economic gain for the employer and employee alike, and for the government concerned. But new problems have arisen because of the comparative ease with which crews have access on board ship to penicillin given parenterally or orally for therapeutic and prophylactic purposes; this has made post-treatment control and follow-up more complicated.

The problem of immediate importance in maritime venereal-disease control is early syphilis. In some maritime countries, the incidence of early syphilis has been less noticeable in port than in inland areas; but, on the other hand, increasingly important ports in underdeveloped areas remain very real foci of infection at a time when the tonnage of post-war merchant fleets has

[11] *Wld Hlth Org. techn. Rep. Ser.* 1950, 20

risen by 10% since 1946, and is now, according to the Lloyds Register for 1952, a total of 90,868,495 gross tons. In the light of this steady increase in tonnage and in floating population, the problem of venereal diseases is likely to hold the interest of maritime nations throughout the world; and health administrations may wish further international action with regard to this truly international problem.

INTERNATIONAL EXCHANGE OF TECHNICAL INFORMATION

The exchange of technical information is of immense value to countries, and its promotion and execution are, therefore, a basic function of WHO. In effect, the Organization acts as an international clearing-house for this purpose. It is essential that the latest information on progress in the prevention, diagnosis, treatment, and other aspects of treponematosis control be made available to all interested countries, so that control activities may be in step with the march of events. Much information is always obtainable from current medical literature, but the programmes of health administrations and of WHO yield important data which can best be made known through the Organization. In addition, as a result of its operational studies, and as a co-ordinator of international research, WHO is an important source of knowledge on specific subjects of wide interest.

Expert Committees and Advisory Panels

In recommending technical policies, as well as in advising governments on measures concerning treponematosis control, WHO must be able to call upon the technical advice of persons who are not only most competent in their field, but also representative of the newest trends and of as wide a geographical distribution as possible. This last consideration is in line with the international character of the Organization; it also serves another important purpose : experience has demonstrated that methods of combating a disease that may be efficient and effective in one country may have little practical value as long as they are not tested and accepted by other countries with similar problems. It is therefore essential when drawing up overall plans for control of a disease to have the benefit of expert views, representative at the same time of various technical aspects and of national methods of control. It is principally for this purpose that WHO has established a series of expert advisory panels, each concerned with specific problems.

Technical guidance in WHO's treponematoses activities is provided by an Expert Advisory Panel on Venereal Infections and Treponematoses, the members of which are appointed by the Director-General because of their competence in this particular branch of medicine, and by expert committees, the members of which are drawn from the panel and the composition of which varies according to the subject chosen for consideration at a particular committee session. At the present time, WHO has an expert advisory panel of 73 members, from 44 countries, upon whose technical knowledge and experience in the treponematoses it may draw.

Four expert committee meetings have been held—two in 1948 and one each in 1949 and 1952. A Subcommittee on Serology and Laboratory Aspects has also held three sessions—in 1949, 1950, and 1953. The tech-

nical reports of these groups have furnished the basis for WHO work against the treponematoses; they are also a valuable source of up-to-date technical information for physicians, public-health authorities, and others interested in treponematoses control.

Symposia and Other Conferences

WHO fosters exchange of technical information by sponsoring symposia and other international conferences. Such meetings bring together leading specialists from different countries and make possible direct professional contact and exchange of views. For example, an international symposium on syphilis was organized in Helsinki in 1950 [12] and was attended by 28 participants from six countries; in the same year, a larger symposium, at which participants numbered 76 and represented 12 countries, was held in Paris.[13] These symposia did much to reorient European medical opinion with regard to the new trends in the treatment of syphilis and to hasten the transition from metal chemotherapy to therapy based on penicillin.

In 1952, an international symposium on yaws control was held in Bangkok and was attended by 39 participants from 23 countries. This symposium covered every phase of yaws control and provided an important forum for the exchange of experiences in the large yaws-control projects getting under way in several parts of the world. The technical information which was presented at the symposium was subsequently published in a WHO monograph.[14]

An earlier and different type of activity was that represented by the WHO Syphilis Study Commission to the USA, in which a group of specialists from seven countries spent several months of 1949 in the USA to investigate and evaluate the use of penicillin in the syphilis-control programme of the USA as organized by the US Public Health Service. The Commission also observed other aspects of the programme in the USA, among them the technique of contact interviewing and the training of contact interviewers, the morbidity and epidemiological report forms and the mechanical methods used in their filing and analysis, and the inpatient facilities provided by rapid-treatment centres and the education of the patients carried out therein.

The Commission concluded that the venereal-disease-control methods used in the USA could well serve as a guide in planning future programmes elsewhere, provided that they were suitably adapted to local conditions and requirements; that the value of penicillin in the treatment of syphilis was an outstanding USA discovery; and that the USA was, at that time, the place of choice for the study of venereal-disease problems and control methods. The results of the Commission's study were published in the WHO Technical Report Series.[15]

Consultant Aid

Another, more direct, method of exchanging technical information is seen when the Organization provides an expert adviser or consultant for a national health administration. Such technical personnel may be members of the staff of WHO headquarters or of the regional offices, or may be experts recruited for assignment to a specific project for a shorter or longer period. The provision of expert advice in this way has been found a most useful type of WHO assistance, both in demonstration and training projects and

[12] *Transactions of the International Symposium on the Study of Syphilis* (1951) Helsinki (*Acta derm.-venereol. (Stockh.)* Supplementum 24)

[13] Organisation Mondiale de la Santé (1951) *Colloque International sur la Syphilis*, Paris

[14] World Health Organization (1953) *First International Symposium on Yaws Control*, Geneva (*World Health Organization : Monograph Series* No. 15)

[15] *Wld Hlth Org. techn. Rep. Ser.* 1950, 15

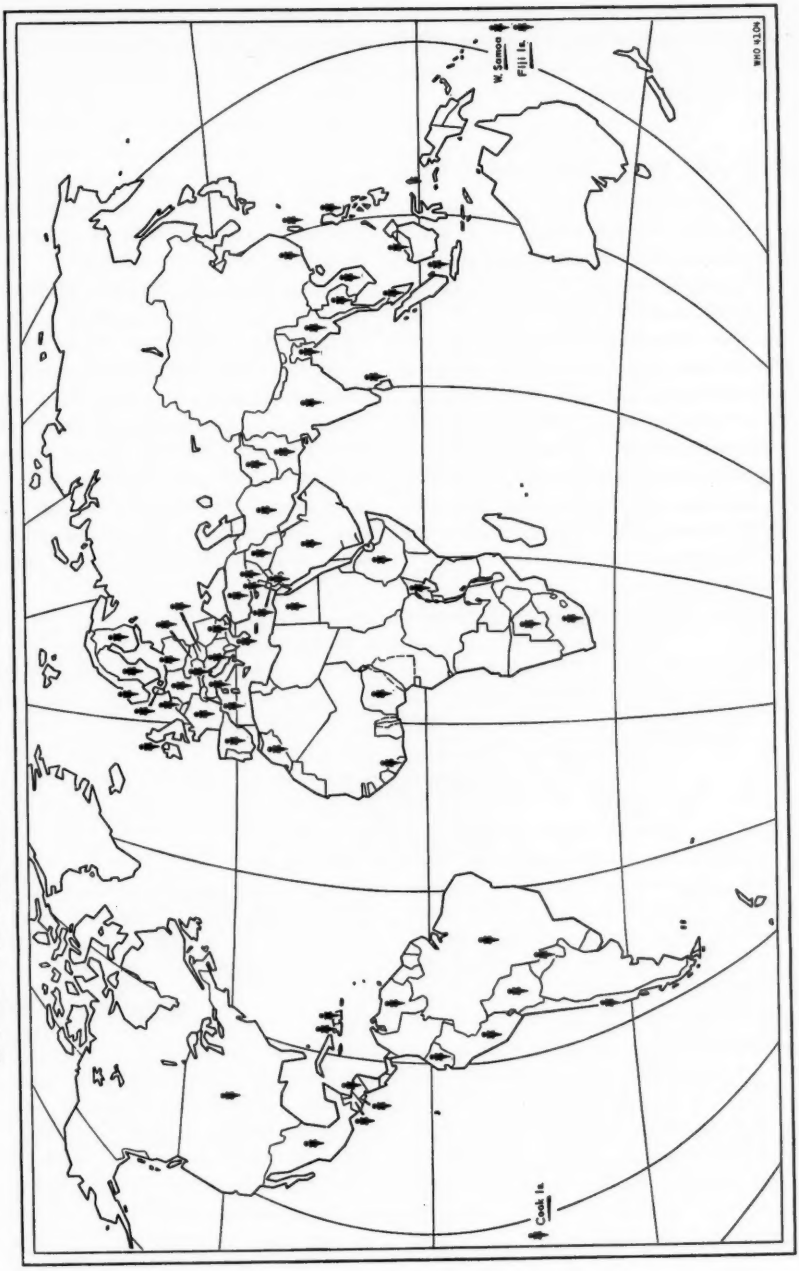


FIG. 24. ACTIVITIES OF WHO TREPONEMATOSES CONSULTANTS AND ADVISERS, 1948-53

in mass campaigns. The countries which requested and received the services of WHO consultants and advisers during the period 1948-53 are shown in fig. 24.

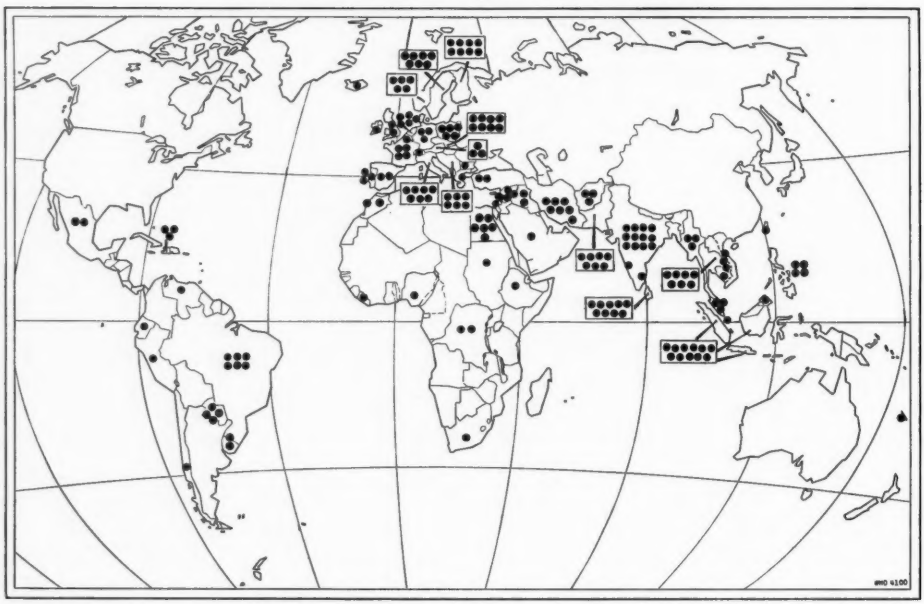
Fellowships and Other Professional Training Activities

The awarding of fellowships and travel grants has become an important and valuable form of Organizational aid to health administrations and to individuals. In the years 1947-53, 196 fellowships and travel grants concerned with the control of venereal diseases and treponematoses were awarded (fig. 25), at a cost of approximately a quarter of a million dollars. The distribution according to WHO Regions was as follows : Africa, 5; the Americas, 21; South-East Asia, 47; Europe, 78; Eastern Mediterranean, 30; and Western Pacific, 15.

In some instances, the training has been in general public-health methods; in others, Fellows have studied syphilis control in clinics or at the city, provincial, or national level; in others again, laboratory aspects or mass campaign practices have been the subjects of study. Many of the fellowships have been granted in co-operation with UNICEF, as part of national treponematoses projects.

The awarding of fellowships supplements the activities of demonstration and training centres, and fellowship funds are usually included in such projects in order to provide the best available training for the medical officers and technical personnel who will bear the responsibility for developing the projects after the withdrawal of WHO assistance. Fellowships and travel grants have also been given for studies abroad which will serve WHO's ultimate purpose of

FIG. 25. DISTRIBUTION OF 196 TREPONEMATOSIS FELLOWSHIPS, BY COUNTRIES OF ORIGIN, FROM 1947 TO 1953



strengthening the health services of nations, and for bringing participants to symposia and international conferences in which WHO has had an interest.

A number of special training courses have been organized with the assistance of WHO. In Simla, Himachal Pradesh, India, teams—composed of a venereologist, a laboratory technician, and a public-health nurse—from different parts of the country were trained, as groups, in venereal-disease-control methods. A field seminar organized in connexion with the international yaws symposium in Bangkok was another type of group training. A third example is the group-training courses in maritime venereal-disease control at the port demonstration project in Rotterdam.

WHO has also awarded a limited number of grants to universities and laboratories in support of work which has a direct bearing on the activities of health administrations and on WHO programmes. For example, grants have been made to the WHO Serological Reference Laboratory at the Statens Seruminstitut, Copenhagen, and to the International Treponematosis Laboratory Center at Johns Hopkins University, Baltimore, Md., USA. The activities of these centres are reviewed in a later section (pages 97 and 100). It should be mentioned here, however, that these laboratories also serve to train laboratory workers and technicians sent to them either by WHO or by other interested national and international organizations.

Technical Documentation

One of the principal means of disseminating information is represented by WHO publications and technical documents, through which the Organization makes available the information resulting from its own work.

Treponematologists and public-health workers will find information of interest to them particularly in three of the Organization's publications—the Technical Report Series, the Monograph Series, and the *Bulletin of the World Health Organization.* The reports of the WHO Expert Committee on Venereal Infections and Treponematoses and of its Subcommittee on Serology and Laboratory Aspects, and the collective views of other groups of experts, such as the WHO Syphilis Study Commission to the USA, will be found in the Technical Report Series. Extensive studies which are considered to have lasting value and which are of wide general interest, but which do not present a collective view of a problem, are included in the Monograph Series. This series contains either epidemiological or clinical studies on one specific subject by one individual author—such as the monograph *The epidemiology and control of endemic syphilis : report on a mass-treatment campaign in Bosnia*—or a collection of papers by a number of contributors on a certain topic—such as the selection of papers submitted at the First International Symposium on Yaws Control. Finally, the *Bulletin* contains in each volume a number of scientific papers prepared either by epidemiologists, clinicians, or public-health workers who carry out assignments directly under the auspices of the Organization, or by outside contributors who wish to give their original findings a wide international distribution.

Information included by WHO in any of these publications has always to meet certain special requirements. First and most specific of these is that it should have " international significance ". It is one of the principles of the WHO publications programme that a paper should not be included in an Organization publication if a more suitable vehicle for it exists. Although the expression " international significance " is not easily defined, it is meant, in general, to distinguish information which, in contradistinction to that of a purely local or national interest, is likely to be of practical value to health workers in a number of countries, or to

represent the achievements of international co-operation in the field of health. Studies of results in specific disease-control methods which may be readily applied, with modifications, to all countries; surveys of the geographical distribution of diseases; and review articles prepared by outstanding experts on the basis of literature from all countries which have contributed to existing knowledge—these are among the types of articles which may be considered to be internationally significant. In addition, reports of surveys on specific subjects made by expert consultants on behalf of WHO, after conferring with relevant workers in various countries, and personal investigations covering wide areas, as well as reports or original findings made in the course of WHO field programmes, are considered to have international significance, because they are essentially the outcome of international co-operation. In following this editorial policy, the Organization endeavours to make a distinctive contribution to medical documentation by providing the research worker, the epidemiologist, the clinician, and the health administrator with technical information to which he might not otherwise have access.

Experience has shown that another noteworthy source of technical information is to be found in papers issued by the Organization in limited number as mimeographed documents. Such documents are intended primarily for members of expert advisory panels or committees and for internal use by the staff or by laboratory and research institutes with which the Organization has close working relationships. These documents can be made available to interested persons, but they are not destined for library files or meant to be indexed in reference lists or reviewed by medical journals. Papers which are considered of more lasting and general value are often included in one of the WHO technical publications, as has already been noted.

A list of WHO reports, monographs, articles, and other publications on the treponematoses may be found on page 108.

INTERNATIONAL CO-ORDINATION OF RESEARCH

The co-ordination and promotion of research on health problems are among the functions of WHO, particularly when such research is directly related to Organization programmes or projects. Such international research can be accomplished by special field studies or by supporting existing institutions. The present article attempts to give some idea of WHO's research activities relative to the treponematoses and their control.

Operational research and special investigations are carried out to appraise the use and usefulness of various treponematosis-control practices in individual projects. For example, work is under way to evaluate the epidemiological and other data accumulated in the campaign against endemic syphilis in Bosnia. This study is based on a mechanical, punch-card system established at the Central Syphilis Register in Sarajevo, where copies of all field records of the entire campaign are available.

As was mentioned earlier, comparative studies of PAM and the new repository benzylamine penicillin salts in syphilis, yaws, and pinta are being co-ordinated by WHO, in co-operation with leading national experts in several countries. The purpose of these investigations, in which members of the WHO Expert Advisory Panel on Venereal Infections

and Treponematoses from 18 countries are participating, is to evaluate the possible advantages and disadvantages of the use of the new types of penicillin in individual patients, both in clinic practice and in mass campaigns. These studies are in many ways parallel to the operational research undertaken when PAM was first introduced in the treatment of the treponematoses, and when subsequent simplification of injection techniques and dosage schedules were evaluated. Such research as an integral part of WHO projects is profitable, for the modifications which may result in health techniques and campaign procedures can mean greater efficacy at less cost in selective public-health programmes.

Another study assisted by WHO is the appraisal of extensive material made available by the Clinical Co-operative Group in Great Britain. A number of venereal-disease clinics there have pooled follow-up data on different methods of syphilis treatment, in the comparative evaluation of which WHO is assisting.

Similarly, WHO undertook in 1952 to compile information on current practices in leading venereal-disease clinics and among venereologists throughout the world in the treatment of early syphilis. This study, which ended late in 1953, and the results of which will be published in 1954, indicated a very clear general trend towards reliance on penicillin alone : more than 80% of the 277 venereologists participating in the investigation have adopted penicillin treatment without adjuvant therapy.

THE INTERNATIONAL TREPONEMATOSIS LABORATORY CENTER

The International Treponematosis Laboratory Center was established with WHO assistance at Johns Hopkins University, Baltimore, in October 1950. The Center undertakes investigations of certain fundamental problems which can be handled only in a special research laboratory. Also, as previously noted, it serves to train specialists and technicians from various countries under the WHO fellowship programme and under programmes of other institutions interested in laboratory research. Much interesting and important work is being done, the significance of which increases as the years go by.

The first step was to isolate active strains of treponemes from various WHO treponematosis programmes in different parts of the world so that they could be used for comparative studies.[16] Infected material has been prepared by members of WHO field teams, inoculated into rabbits or hamsters, and forwarded by air to the Center. So far, 12 of the 16 strains obtained from patients with venereal or endemic syphilis in Chicago, Mexico, Iraq, and Bosnia, from cases of bejel in Syria and Iraq, and from yaws patients in Thailand, Haiti, Indonesia, and Samoa have been successfully perpetuated in rabbits or hamsters. No pinta strain has thus far been successfully established in experimental animals.

It has been observed that there are persistent differences between and within established types and strains of treponemes. It appears that these differences are quantitative rather than qualitative, and it is believed that the characteristics of a particular strain are based primarily on its capacity to produce hyaluronic acid. The possible influence of environmental factors, including temperature, on the characteristics of types and strains of treponemes is also being studied at the Center. It has long been known that hot summer weather modifies the course of syphilis in experimental animals; the influence of temperature on the development of skin lesions

[16] Turner, T. B., Hollander, D. H. & Schaeffer, K. (1953) *Bull. Wld Hlth Org.* 8, 7

is of special interest, warmth having an inhibitory effect during the incubation period of syphilis. Such studies are particularly interesting in view of the " unitarian " theory that the differences among the treponemes causing syphilis, yaws, bejel, etc., may result from one single ancestral type of treponeme's having adapted itself to different environmental conditions.

Problems of the immunological relationship of different strains of treponemes are also being studied, as are the degree of immunity built up in infected rabbits, judged by their reaction to challenge with another strain, the relationship between specific antibodies, and the development of antibodies during the course of infection. A substantial degree of cross-immunity among the various strains of treponemes has been demonstrated, although the results with bejel and yaws strains are less clear than with different strains of syphilis. It has also been shown by cross-immunity studies using the *Treponema pallidum* immobilization (TPI) test that a close antigenic relationship among the treponemes is probable.

A new treponemal agglutination (TPA) test has been developed by the Center, the Naval Medical Research Institute in Bethesda, Md., and the Venereal Disease Experimental Laboratory at Chapel Hill, N.C. The agglutination of killed *T. pallidum* by the sera of syphilitic individuals had previously been attempted with varying success by a number of investigators but had not proved valuable as a diagnostic procedure owing to difficulties in maintaining a suitable suspension of viable organisms. A procedure has now been found which eliminates these difficulties, and preliminary studies with rabbit sera have shown a high degree of correlation between positive agglutination and the presence of syphilitic infection. Results with human sera have also been encouraging when suitable techniques have been used. A number of laboratory studies on this problem are now being co-ordinated through WHO.

Another discovery at the Center has been the " adherence-disappearance phenomenon " which has been described in a recent publication.[17] Specific techniques developed in connexion with this phenomenon have shown the presence of another specific antibody in the serum of infected individuals which is different from the reagins detected by the usual flocculation or complement-fixation techniques.

The Center has carried out many important comparative studies on the penicillin sensitivity of treponeme strains received from various WHO field projects in order to watch for the possible appearance of penicillin resistance, a question clearly of great significance both to the medical world in general and to the mass campaigns under way against the treponematoses. The Center has also been conducting investigations on the potential efficacy of antibiotics other than penicillin against treponemes; these experiments have shown that, though all the drugs tested have some activity against *T. pallidum*, penicillin is still the most effective known agent against treponemes.

INTERNATIONAL STANDARDIZATION OF SEROLOGICAL REAGENTS AND METHODS

The effectiveness of treponematosis-control programmes depends to a certain extent upon the efficient conduct of serological tests, whether it be a question of the evaluation of the results in the treatment of syphilitic seafarers or of the comparative appraisal of results of mass treatment campaigns against yaws, as carried out in pilot and control areas of such campaigns. The laboratory remains essential to the work

[17] Nelson, R. A., jr. (1952) *Presse méd.* 60, 1719

of the venereologist, the treponematologist, and the medical officer concerned with the control of venereal diseases and of the non-venereal treponematoses.

One of the basic changes in outlook in laboratory work in recent years has been the definition by WHO of the specificity of serological tests in terms of the treponemal diseases as a group rather than in terms of syphilis, as was the case before 1952. However, any conventional antigen for syphilis and the other treponemal diseases can, under certain conditions, give a false-positive result. If different serological techniques are applied, a quantitative reagin titre in one country will not necessarily be comparable with that in another or, for that matter, with that in another laboratory in the same country.

This is due not only to variations of method. Results cannot be standardized by competitive serological conferences between authors of serological tests, since variations in testing procedures the world over are considerable, and particularly since the composition of antigens used and their reactivity also differ widely. In the past, serologists endeavoured to measure one unknown—the titre or the amount of reagin—by two others—either a variety of reagents (of which the constituents were largely unknown) or a variety of methods (for which there were no standards whereby their performance could be judged). The aim of WHO has therefore been to work towards the standardization of the two basic unknowns which might be controlled—the reagents and the methods—so that the unknown titre or reagin can be more accurately and uniformly measured. In 1949, a WHO Serological Reference Laboratory was set up at the Statens Seruminstitut in Copenhagen to conduct a series of studies which might lead to the desired degree of standardization of reagents and methods. (A review of the Laboratory's work will be found on the next page.)

Standardization of antigens

Standardization of antigens has become feasible with the development in recent years of defined substances, namely cardiolipin and lecithin, which replaced the more uncertain lipoidal antigens obtained in the past from animal tissues. The more specific cardiolipin antigens have now been accepted everywhere as the antigens of choice in the serodiagnosis of the treponematoses.

After several years of laboratory studies by members of the WHO Expert Advisory Panel on the Serological and Laboratory Aspects of Venereal Infections and Treponematoses, WHO in 1951 established international reference preparations of cardiolipin and lecithin, by action of the Expert Committee on Biological Standardization.[18] This has enabled laboratories and manufacturers all over the world to standardize their antigens against a known measure by obtaining samples from the Statens Seruminstitut, Copenhagen. These international reference preparations must, however, be replaced from time to time; and continuous study is therefore required.

A monograph by Mary C. Pangborn, the discoverer of cardiolipin antigen, and her associates at the Division of Laboratories and Research of the New York State Department of Health was published by WHO in 1951.[19] This monograph contains much useful information on the preparation and the chemical and serological testing of these antigens. A revised edition is due in 1954.

Standardization of methods

The establishment of an international reference bank of strongly positive, moderately positive, and weakly positive reacting freeze-dried sera (measured by titre) against

[18] *Wld Hlth Org. techn. Rep. Ser.* (1952) **56**, 8

[19] Pangborn, M. C., Maltaner, F., Tompkins, V. N., Beecher, T., Thompson, W. R. & Flynn, M. R. (1951) *Cardiolipin antigens*, Geneva (*World Health Organization : Monograph Series* No. 6)

which existing serological methods in use anywhere in the world can be compared is the logical second step in the standardization work of the WHO Reference Laboratory at Copenhagen.

The work on freeze-drying has been carried out by a number of laboratories (Bombay, Caracas, Coonoor, Johannesburg, London, Madras, Naples, and Osaka) in co-operation with the Copenhagen Laboratory, which has, in turn, sent sera for testing to 15 laboratories in different parts of the world (Albany, Bergen, Bombay, Cairo, Calcutta, Caracas, Chamblee, Coonoor, Johannesburg, London, Naples, New York, Osaka, Tel Aviv, and Trondheim) so as to ensure as wide a basis as possible for the planned reference bank.

At the seventh session of the WHO Expert Committee on Biological Standardization, held in 1953, it was decided that the stability of freeze-dried sera had been proved in the preparatory studies carried out by the co-operating laboratories and that actual international reference preparations could now be established. Action is being taken accordingly; and it will therefore be possible, in the course of 1954, for national laboratories all over the world to obtain samples of international reference sera from Copenhagen—enabling them to guide serological workers in their countries in carrying out tests with a defined degree of seroreactivity, determined by the titres of the freeze-dried sera—in addition to obtaining defined cardiolipin antigen reference preparations.

Standardization of methods has also been fostered by the inter-laboratory exchange of sera for other purposes, for instance, for determining the stability of sera in postal transmission. Twenty-six laboratories (Montreal, Ottawa, Albany, New York, Copenhagen, Chamblee, Havana, Mexico, Montevideo, Reykjavik, Lisbon, London, Brussels, Bergen, Zurich, Palermo, Vienna, Helsinki, Ankara, Tel Aviv, Cairo, Baghdad, Teheran, Calcutta, Colombo, and Jogjakarta) and a number of WHO field teams (e.g., in Guatemala, Simla, and Bangkok) have participated in various studies of this kind.

Parallel work has been undertaken by the Venereal Disease Research Laboratory and Training Center in Guatemala, which has aimed at the standardization of serological tests in Central America under the auspices of the Pan American Sanitary Bureau and WHO. Assistance in serological work has also been given in that part of the world by a number of training courses, which have been attended by many technicians from most of the Central American countries. The influence of these courses has already shown itself in the syphilis-control programmes in the Americas.

As already mentioned, much of the work in standardization of serological reagents and methods has been carried out by the WHO Serological Reference Laboratory in Copenhagen, in co-operation with a number of national laboratories. To illustrate the type of work undertaken at the Laboratory, a review of some of its activities is given below.

THE WHO SEROLOGICAL REFERENCE LABORATORY

The work of the WHO Serological Reference Laboratory, Copenhagen, falls under four principal headings : (1) evaluation of antigens for the serodiagnosis of syphilis, (2) testing samples of blood or serum transmitted to the Laboratory, (3) research work on serodiagnostic methods, and (4) training of personnel in the use of serodiagnostic methods. In return for this work, WHO makes a yearly grant to the Laboratory.

Three different categories of antigen have been tested : (*a*) antigen used, or to be used, by WHO field teams (work with this type of antigen has predominated); (*b*) antigen from producers (only in a few instances have such

cases been dealt with, and if so only for orientation purposes); and (*c*) antigen prepared at the Laboratory from the provisional international reference preparations of cardiolipin and lecithins of 1951 and 1953.

The research work on serodiagnostic methods is concerned with lipid antigens, on the one hand, and the TPI test, on the other.

Shortly after the publication of the WHO monograph on cardiolipin antigens (see page 99), the serological techniques described therein were tried out with a view to perfecting their performance. The purpose was to enable tests for the acceptance or rejection of new lots of cardiolipin and lecithin to be performed by similar methods at the Division of Laboratories and Research of the New York State Department of Health, Albany, N.Y., and at the Statens Seruminstitut, Copenhagen.

Preliminary studies on the keeping qualities of lecithins and cardiolipin antigens have been performed with the Copenhagen complement-fixation technique. Using this test method, new lots of cardiolipin and lecithins have been compared with the provisional international reference preparations of cardiolipin and lecithins for 1951.

Cardiolipin antigens have been compared with crude lipid antigens, using different types of seroreactions, such as complement-fixation, tube flocculation, and slide flocculation; the maturation phenomenon of cardiolipin antigens has been studied in complement-fixation experiments and by nephelometric methods; and the results of the various studies have been evaluated in close collaboration with the Statistical Department of the Statens Seruminstitut.

In September 1952, the Laboratory was invited by WHO to take part in a co-operative study on the TPI test. The first WHO TPI control serum was prepared in Copenhagen; it was distributed to 25 laboratories in March 1953. Preliminary quantitative results from ten laboratories (Copenhagen, Washington, Lyon, Palermo, Bordeaux, Paris (2), Landstuhl, Lille, and Chamblee) were compiled at the Laboratory in July 1953, and it was found that the variation in titre was great, suggesting the need for further investigation.

Rabbits inoculated with *T. pallidum* (Nichols' pathogenic strain) have been sent to six different laboratories in Europe. The attainment of optimal survival conditions for pathogenic *T. pallidum* in vitro has been, and still is, subject to intense study.

In November 1950, 14 specimens of blood, mainly from syphilitics, were collected, and freeze-dried serum was prepared for use in a preliminary experiment in which the suitability of freeze-dried serum for serological evaluation, as well as the keeping quality at different temperatures, was tested in the Copenhagen Laboratory and in laboratories in the following cities : Bergen, Calcutta, Chamblee, London, and Tel Aviv. This pilot experiment resulted in the recommendation that further studies on the value of freeze-dried sera in the evaluation of serological methods be undertaken. It was decided that 80 sera from selected donors (syphilitic and non-syphilitic) should be freeze-dried. The Laboratory has thus far prepared 19 freeze-dried sera and has collected an additional 28 sera from other laboratories. Early in 1953, samples of the first 30 sera (some in duplicate) were sent out to a number of laboratories of members of the Expert Advisory Panel on Serology and Laboratory Aspects.

In March 1951, the WHO Reference Laboratory was requested to take part in the chemical analysis of samples of cardiolipin and lecithin for the Expert Committee on the Unification of Pharmacopoeias. Specifically, the Laboratory undertook the phosphorus analysis and the determination of dry weight. In 1953, the chemical results from other laboratories were studied.

TREPONEMATOSIS CONTROL AS A MEANS TO AN END

Health activities as a means of international co-operation are not new but can be traced as far back as the 14th century. However, there has been a significant change in emphasis and objectives since those early times. From the dissemination of information and the setting-up of quarantine regulations to prevent the spread of pestilential diseases from one country to another, international health activities have been extended to the pooling of knowledge, experience, and resources to provide direct assistance to countries in communicable-disease control and in the general promotion of the health of their people. A principal objective has now become the control and eventual elimination of diseases of public-health importance wherever they occur.

Like most other projects of assistance to governments, treponematosis control, whether it be through an urban programme for the control of venereal syphilis, based on stationary clinics, or through a mass campaign against a non-venereal treponematosis in a rural area, can also serve as a bridgehead for the development of local health services. At some point in the treponematosis-control programme, the gains should be consolidated as part of general communicable-disease control. The activities required to keep the infection at a controllable level—or to eliminate it completely—should be integrated into the local or national health services. This integration represents a new challenge in modern public-health work. As the need for intensive treponematosis-control measures diminishes, general public-health activities of gradually increasing scope may then take precedence over the fight against this specific infection. Through long-term planning, treponematosis control may thus become a means to an end—namely, the strengthening of local health services.

CONSOLIDATION OF RESULTS

The more specific objectives of international co-operation in treponematosis control have already been outlined (page 67), and the contributions which selective public-health projects against these infections can make towards "the highest attainable standard of health"[1] have been suggested. However, any group of public-health workers which attains a high degree of specialization may sometimes tend to overlook the fact that, in the final analysis, its work will be productive only if supported by a general programme of disease prevention. Work in conjunction with other health activities (maternal and child health, malaria, tuberculosis, etc.) is desirable whenever initial exploration of the health problems in an area shows technical and administrative advantages. As has already been mentioned, selective public-health projects are potential bridgeheads for extension into broader, multiphasic, public-health activities both in urban and rural areas and provide a method of strengthening the structure of local, as well as national, health services—a basic aim of WHO.[2]

In the past, the advantages and disadvantages of the approach to disease control and to the improvement of health in general by the stationary urban clinic and rural health centre system have been realized. But little information on mass campaigns has been available until recent years, when extensive malaria-, tuberculosis-, and treponematosis-control activities have been undertaken by health administrations with international assistance.

That the non-venereal treponematoses can be controlled by mass application of penicillin is indicated by the results observed in resurveys conducted in a number of sample and control areas. This is illustrated for yaws in table VII; for endemic syphilis, the evidence already given in table VI (page 77) and fig. 18 (pages 78-9) speaks for itself. In other instances, the results have been less good, and the number of new cases represented by reinfections, infectious relapses, or cases reintroduced from neighbouring areas has caused some concern. This question is to some extent connected with the intensity of the treatment of household and community contacts in the different projects.

TABLE VII. RESULTS OF SAMPLE RESURVEYS AFTER 6-12 MONTHS IN CONTROL AREAS OF FOUR YAWS-CONTROL PROJECTS

Project area		Number examined	Cases of yaws	
			number	%
Haiti	1st survey	9,752	4,160	42.6
	2nd survey	12,915	103	0.8
Indonesia	1st survey	1,632	357	21.9
	2nd survey	1,667	96	5.7
Philippines	1st survey	16,072	2,900	18.0
	2nd survey	16,481	409	2.5
Thailand	1st survey	313,338	56,407	18.0
	2nd survey	353,800	2,241	0.6

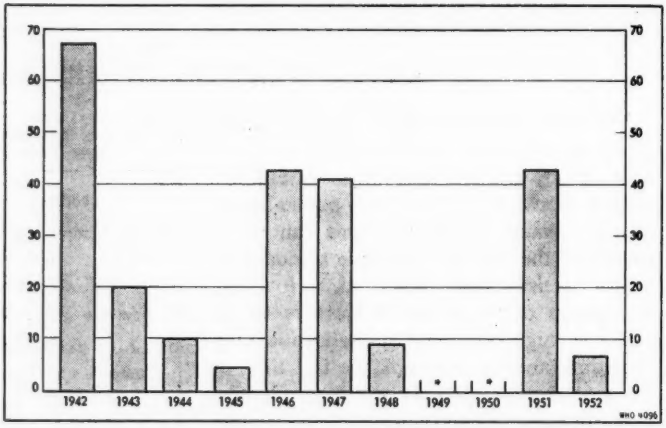
It is evident that the good initial results obtained by a mass "sweep" of the population with penicillin must be followed by resurveys. The mass treatment phase of campaigns against any of the treponematoses is but the first step towards full control and eradication of the infection. Control efforts must be continued even after that phase; follow-up examinations and, where necessary, re-treatment must be carried out if the benefits of the original action are not to be lost.[3] Governments must provide for this continuity in their planning and in drawing up their budgets. Past, and ultimately unsuccess-

[1] From preamble to the Constitution of the World Health Organization. In: World Health Organization (1953) *Handbook of basic documents*, Geneva, 6th edition, p. 3

[2] Bonne, W. M. Guthe, T. & Reynolds, F. W. (1953) *Bull. Wld Hlth Org.* 8, 371

[3] Guthe, T., Reynolds, F. W., Krag. P, and Willcox, R. R. (1953) *Brit. med. J.* 1, 594

FIG. 26. INCIDENCE OF YAWS IN HARKERS HALL AREA, ST. CATHERINE, JAMAICA



Ordinates : attack-rate per 1,000 inhabitants

Mass treatment was carried out during the years 1942-45, 1947, and 1951-52; but the results were not consolidated, and the efforts were thus largely wasted.

* *No data are available for the years 1949-50*

ful, eradication campaigns have made this abundantly clear; the rise and fall in the incidence of yaws shown in fig. 26 are due largely to insufficient follow-up measures. When the reservoir of infection has been sufficiently reduced, the consolidation of the results may be continued under general public-health programmes. This will, of course, depend on the existence or creation of permanent rural health facilities in the areas concerned. It should be possible for health administrations to take advantage of the progress made and to reinforce the rural health administrations with staff previously engaged in the mass campaigns. Further planning by health administrations, WHO, and UNICEF is needed if vast efforts and funds are not to be wasted and if recurrence of the treponematoses in endemic or hyper-endemic form is to be avoided.

Whether the victory will be final also depends on the degree of social advancement in the areas treated. The epidemiological environment is changed by mass treatment, but there must also be a corresponding change in the social environment—and that as soon as possible—if it is not to contribute to a recurrence of the spread of the treponematoses. What has taken many countries centuries to achieve in the past can now take place in a few decades. There is good reason to hope that the mass campaigns themselves contribute substantially to the health education of the public, through the convincing complete disappearance of lesions and the rapid cure.

Parallel health projects in fields other than the treponematoses also help substantially towards this change in the social environment, which, it should be said, has already begun in many areas. WHO is concerned with all aspects of public health and social medicine, and especially with the training of personnel in preventive medicine and hygiene. Considerable success is being achieved in the control of malaria and other insect-borne diseases, such as yellow fever. Immunization against tuberculosis with BCG is widespread; in some areas, immunization projects against diphtheria and pertussis have been encouraged. Epidemics of poliomyelitis and influenza call for prompt action and research. Health education and activities in maternal and child health, nutrition, and social and occupational health are being promoted; and problems such as drug addiction and chronic diseases are not excluded from consideration. Achievements in such a variety of fields cannot fail to leave an impression in underdeveloped areas.

ECONOMIC ASPECTS OF TREPONEMATOSES CONTROL

The economic value of the health of its inhabitants to a community is a subject which is receiving the increasing attention of governments. Studies on this subject are still insufficient, particularly as regards the less-developed areas; but attempts to translate health into terms of economic productivity and gain have shown how serious are the losses attributed to ill health and how profitable can be action against them. Such attempts can be only approximations, yet they have provided a basis for interesting and stimulating discussion.

Several illustrations of this thesis are provided by the treponematoses. It has been estimated that 100,000 man-days of labour are lost annually as a result of venereal diseases in Southern Rhodesia;[4] and, in Haiti, where yaws was widely prevalent among the rural population, the 35,000 to 55,000 persons treated monthly in the joint WHO/UNICEF programme have meant the return to work of approximately 100,000 incapacitated persons and a consequent increase in national production of $5,000,000 a year.[5]

In some countries it has been possible to estimate directly the loss of manpower attributable to venereal syphilis in military forces, civilian life, and industry, and to calculate the cost of institutional care of late syphilitics. Thus, the disability and cost to the nation from syphilis in the USA is illustrated on page 107.[6] Efforts have also been made to calculate indirectly the value of certain preventive measures, such as obligatory premarital serological examinations : in the State of California, for example, it was estimated that, for the years 1949, 1950, and 1951, a total loss of $6,339,274 in productive manpower and domiciliary care was prevented by this screening method, and that this meant a yearly saving to the State of $1,275,364.[7]

The economic loss caused by the treponematoses is reflected in the age groups from which they take their toll in the form of incapacitation, invalidism, or the need for special medical care. It is obvious that infancy and early childhood are a period of investment for the family and community. It is considered, for example, that in the USA the non-productive phase of life extends to the age of 18 years and that this period entails an investment in the child up to that age of more than $7,000 for a family with an annual income of $2,500.[8] In other countries, particularly in agricultural areas and where child labour in industry is common, the child begins to be productive at a much earlier age; even so, it is almost certain that up to the age of 15 years the investment in a child greatly exceeds the economic return.

What does this mean in populations in which yaws or other treponematoses are prevalent ? It has already been pointed out (page 49) that the age distribution of the non-venereal treponematoses is different from that of venereally acquired syphilis, since the former are primarily diseases of childhood, while the latter affects those who have reached sexual maturity. This is illustrated

[4] Winslow, C.-E. A. (1951) *The cost of sickness and the price of health*, Geneva (*World Health Organization : Monograph Series* No. 7) p. 30

[5] US Department of State (1950) *Point four : cooperative program for aid in the development of economically underdeveloped areas*, Washington, D.C. (Publication 3719, Economic Cooperation Series 24)

[6] Federal Security Agency, Public Health Service (1952) VD Fact Sheet, Division of Venereal Disease, Office of Statistics, Issue number 9

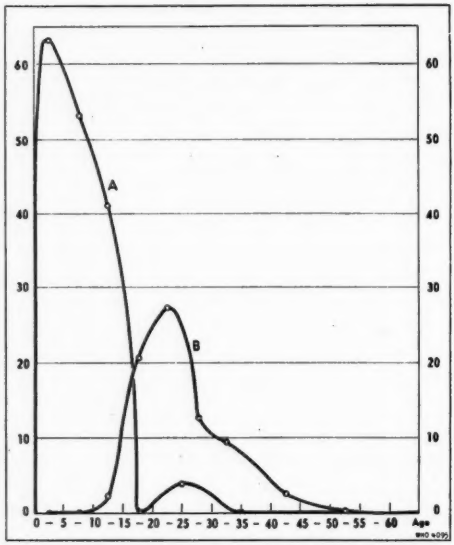
[7] Condit, P. K. & Brewer, A. F. (1953) *Amer. J. publ. Hlth*, 43, 880

[8] Dublin, L. I., Lotka, A. J. & Spiegelman, M. (1947) *The money value of a man*, New York, p. 50

in fig. 27, based, for yaws, on material from an area in Jamaica [9] and, for venereal syphilis, on data for an urban area in the USA (Baltimore).[10] It will be seen that more than 42.5 persons per 1,000 had acquired yaws before the age of 15, and that the attack-rate after that age was only 1.5 per 1,000. In venereal syphilis, on the other hand, the rate was only 2.12 per 1,000 among those under 15 years of age and much higher thereafter. From a social and economic standpoint, however, the result in terms of productive manpower is the same : in yaws, the early onset of the disease results in a variety of disfiguring and invaliding manifestations, including locked ankles and elbows and plantar and palmar lesions, during the most productive years of life; in venereal syphilis, the productive age-groups are attacked directly, with consequent immediate absenteeism and incapacitation for work, and with neurological, cardiovascular, and other systemic involvement which later causes a further important loss of manpower if the disease is untreated.

Another economic factor is the neonatal mortality attributable to the treponematoses. The higher death-rate among congenitally syphilitic infants compared with that of children born of healthy mothers has long been recognized. Moreover, venereal syphilis is known to be the cause of approximately half the stillbirths and abortions in untreated syphilitic women. That this is true to some extent also among pregnant women suffering from endemic syphilis has been contended by Grin.[11] There is some evidence that yaws, too, may result in increased infant mortality,[12] although it is generally believed that this disease does not play an important role as a " natural " population check. Yaws is more of a crippler than a killer, and yaws-control programmes mean that there will be increased manpower for productive purposes rather than more mouths to feed.

FIG. 27. ONSET OF YAWS (JAMAICA) AND DISCOVERY-RATES FOR EARLY SYPHILIS (BALTIMORE) BY AGE GROUPS



Ordinates : annual rates per 1,000 population
A — Yaws in Jamaica
B — Syphilis in Baltimore

Apart from these profit and loss considerations, there are wider logical grounds on which health programmes should form part of general programmes for social and economic development wherever possible. Myrdal,[13] for example, has said :

" It is true that an improved health standard will imply both a more favourable age structure of the population with a larger part of it in the productive ages and, in every age-group, a people more able and

[9] Hill, K. R. (1953) *Non-specific factors in the epidemiology of yaws.* In : World Health Organization, *First International Symposium on Yaws Control*, Geneva (*World Health Organization Monograph Series* No. 15), p. 17

[10] Turner, T. B., Dyar, R., Clark, E. G. & Birkhead, M. F. (1943) *Amer. J. Hyg.* 37, 273

[11] Grin, E. I. (1953) *Epidemiology and control of endemic syphilis : report on a mass-treatment campaign in Bosnia*, Geneva (*World Health Organization : Monograph Series* No. 11), p. 41

[12] Saunders, G. M. & Muench, H. (1937) *Amer. J. Hyg.* 26, 423

[13] Myrdal, G. (1952) *Chron. Wld Hlth Org.* 6, 211

even more willing to work and work well. This by itself tends to raise productivity. It is also true that, according to the principle of cumulative causation . . . an improved health standard will per se always tend to improve all other component factors in the plane of living."

In effect, medical advances can serve as "pacemakers" of social change, a view which was pointed out to the United Nations Social Commission : "In the underdeveloped areas . . . release of the resources of the countries from the tangled undergrowth of mass disease is a prerequisite for development." [14]

The WHO Expert Committee on Venereal Infections and Treponematoses [15] has pointed out : "Penicillin in mass diseases like syphilis and yaws is, indeed, an important pacemaker of this kind . . . "

Millions of people are incapacitated by the treponematoses during the most productive period of their lives, in areas where national development requires able bodies to assist in agricultural, industrial, and other programmes for economic expansion. In such areas the widest possible application of penicillin in treponematosis-control programmes is a means to an end and represents an element in social and economic progress. Much remains to be done, nationally and internationally, but the impact of the work under way has already begun to be discernible in many parts of the world.

[14] United Nations (1952) *Preliminary report on the world social situation with special reference to standards of living*, New York, chapter III, p. 32 (document E/CN.5/267/Rev.1)

[15] *Wld Hlth Org. techn. Rep. Ser.* 1953, 63, 7

DISABILITY FROM, AND COST OF, SYPHILIS IN THE USA*

Estimated disability from syphilis, in man-years

Hospitalization for insanity from syphilis (1950)	42,438
Disability from cardiovascular syphilis, including aneurysm (1949)	12,332
Disability from locomotor ataxia (1949)	2,080
Disability from syphilitic blindness (1949)	39,000

Estimated annual cost of syphilitic psychosis and syphilitic blindness, in US $

Maintenance of patients with syphilitic psychoses (1950)	41,162,000
Loss of income by patients with syphilitic psychoses (1950)	86,489,000
Loss of State and Federal income tax payments from patients with syphilitic psychoses (1950)	6,790,000
Maintenance of syphilitic blind (1949)	18,750,000

* Federal Security Agency, Public Health Service (1952) VD Fact Sheet, Division of Venereal Disease, Office of Statistics, Issue number 9

SELECTIVE WHO BIBLIOGRAPHY ON TREPONEMATOSIS CONTROL

Bulletin of the World Health Organization

1949

GUTHE, T.
Venereal diseases in Ethiopia. *Bull. Wld Hlth Org.* **2**, 85

International control of venereal disease : excerpts from the report on the second session of the Expert Committee on Venereal Diseases. *Bull. Wld Hlth Org.* **2**, 139

MAHONEY, J. F. & ZWALLY, M. R.
Observations on the serodiagnosis of syphilis. *Bull. Wld Hlth Org.* **2**, 227

THOMAS, E. W.
Rapid treatment of syphilis with penicillin: I. A survey of the problem. *Bull. Wld Hlth Org.* **2**, 233

THOMAS, E. W.
Rapid treatment of syphilis with penicillin. II. Penicillin in prenatal and infantile syphilis. *Bull. Wld Hlth Org.* **2**, 249

1950

BEKIERKUNST, A. & MILGROM, F.
Complement-fixation reactions with cardiolipin antigen compared with Kahn reactions. *Bull. Wld. Hlth Org.* **2**, 687

CUTLER, J. C.
Survey of venereal diseases in Afghanistan. *Bull. Wld Hlth Org.* **2**, 689

1951

PANGBORN, M. C., MALTANER, F., TOMPKINS, V. N., BEECHER, T., THOMPSON, W. R. & FLYNN, M. R.
Cardiolipin antigens. *Bull. Wld Hlth Org.* **4**, 151

HILL, K., KODIJAT, R. & SARDADI, M.
Atlas of framboesia : a nomenclature and clinical study of the skin lesions. *Bull. Wld Hlth Org.* **4**, 201

1952

CUTLER, J. C., KVITTINGEN, J., ROSE, E., MCCULLOUGH, J. C., TAMPI, R. B., SEN, S., PARMAR, C. & LAL, G.
Mass treatment of syphilis in an Indian province : report of the World Health Organization Venereal Disease Demonstration Team in the Ghund area of the Himachal Pradesh, India. *Bull. Wld Hlth Org.* **5**, 377

KVITTINGEN, J., MCCULLOUGH, J. C., TAMPI, R. B. & BRALLA, J. J.
Significance of rapid serological testing for syphilis in field surveys. *Bull. Wld Hlth Org.* **5**, 473

KVITTINGEN, J., CUTLER, J. C., GUEVARA, J. A., MCCULLOUGH, J. C., ROSE, E., FORD, V., TAMPI, R. B., SEN, S., LAKSHWIR, KHAN, J. & DASS, P.
Serological tests for syphilis in lepers : tendency for various antigens to give false-positive reactions. *Bull. Wld Hlth Org.* **5**, 481

GHORPADE, K. V.
Comparison of two commercial Meinicke antigens : report on the use of three different qualities of saline in the preparation of each antigen for serological testing. *Bull. Wld Hlth Org.* **5**, 513

GRIN, E. I.
Endemic syphilis in Bosnia : clinical and epidemiological observations on a successful mass-treatment campaign. *Bull. Wld Hlth Org.* **7**, 1

TURNER, T. B. & HOLLANDER, D. H.
Studies on treponemes from cases of endemic syphilis. *Bull. Wld Hlth Org.* **7**, 75

KVITTINGEN, J., CUTLER, J. C., MCCULLOUGH, J. A., ROSE, E., FORD, V., TAMPI, R. B., SEN, S. & LAKSHWIR.
Serological aspects of a syphilis-control programme in the Ghund Area, Himachal Pradesh, India. *Bull. Wld Hlth Org.* **7**, 83

1953

TURNER, T. B., HOLLANDER, D. H. & SCHAEFFER, K.
Biological investigations on treponemes. *Bull. Wld Hlth Org.* **8**, 7

HILL, K. R.
Non-specific factors in the epidemiology of yaws. *Bull. Wld Hlth Org.* **8**, 17

LEVITAN, S., RODRIGUEZ, C., JACOBS, J. C., PETRUS, E. & DURAND, J. B.
The treatment of infectious yaws with one injection of penicillin. *Bull. Wld Hlth Org.* **8**, 55

KITCHEN, D. K. & REIN, C. R.
Time-dose relation in penicillin therapy with special reference to yaws : laboratory basis for effective therapy. *Bull. Wld Hlth Org.* **8**, 77

REIN, C. R. & KITCHEN, D. K.
Time-dose relation in penicillin therapy with special reference to yaws : clinical basis for effective therapy. *Bull. Wld Hlth Org.* **8**, 91

HILL, K. R.
Antibiotics other than penicillin in the treatment of yaws. *Bull. Wld Hlth Org.* **8**, 107

HACKETT, C. J.
Extent and nature of the yaws problem in Africa. *Bull. Wld Hlth Org.* **8**, 129

VAUCEL, M. A.
Le pian dans les territoires africains français. *Bull. Wld Hlth Org.* **8**, 183

JUNGALWALLA, N.
Planning for yaws control in South-East Asia. *Bull. Wld Hlth Org.* **8**, 213

GUIMARÃES, F. N.
Yaws in Brazil. *Bull. Wld Hlth Org.* **8**, 225

REIN, C. R.
Diagnostic aids in mass-treatment campaigns against yaws. *Bull. Wld Hlth Org.* **8**, 245

PETRUS, E., LEVITAN, S., PAOLIELLO, A. & NICOL, R.
La campagne antipianique en Haïti. *Bull. Wld Hlth Org.* **8**, 261

SOETOPO, M. & WASITO, R.
Experience with yaws control in Indonesia : preliminary results with a simplified approach. *Bull. Wld Hlth Org.* **8**, 273

HACKETT, C. J.
Consolidation phase of yaws control : experiences in Africa. *Bull. Wld Hlth Org.* **8**, 299

CRUZ, A. H.
Integration of yaws control into the permanent health structure of the Philippines. *Bull. Wld Hlth Org.* **8**, 345

TROUPIN, J. L., REYNOLDS, F. W. & GUTHE, T.
Yaws control—an opportunity for promoting rural health services. *Bull. Wld Hlth Org.* **8**, 355

BONNE, W. M., GUTHE, T. & REYNOLDS, F. W.
The role of the World Health Organization in yaws control. *Bull. Wld Hlth Org.* **8**, 371

KEENY, S. M.
The role of the United Nations International Children's Emergency Fund in yaws control. *Bull. Wld Hlth Org.* **8**, 379

1949

WRIGHT, R. D. & NICHOLSON, F. P.
Treatment as a factor in the control of the venereal diseases. *Bol. Ofic. sanit. pan-amer.* **28**, 462

COUTTS, W. E.
Organización de la lucha antivenérea : bases principales en que actualmente debe apoyarse una campaña. *Bol. Ofic. sanit. pan-amer.* **28**, 545

1950

ARNOLD, R. C. & MAHONEY, J. F.
Función de los antigenos de cardiolipina en la serologia de la sífilis. *Bol. Ofic. sanit. pan-amer.* **29**, 397

Técnica de floculación en portaobjetos de VDRL : prueba de floculación en tubo de VDRL ; prueba de VDRL para líquido cefalorraquídeo. *Bol. Ofic. sanit. pan-amer.* **29**, 509

THOME, J. V.
Modificaciones que deben hacerse a las actividades educativas antivenéreas de acuerdo con los progresos registrados en su terapéutica con el uso de los antibióticos. *Bol. Ofic. sanit. pan-amer.* **29**, 945

GOODEN, D. R.
Influencia de un programa profiláctico penicilínico en la incidencia de las enfermedades venéreas. *Bol. Ofic. sanit. pan-amer.* **39**, 1051

1951

SAMAME, G.
Profilaxis sistémica antivenérea : informe preliminar sobre el programa de Tijuana, B.C. *Bol. Ofic. sanit. pan-amer.* **30**, 42

CUTLER, J. C. & STOUT, G.
Problemas serológicos en Centro América. *Bol. Ofic. sanit. pan-amer.* **30**, 321

Control o erradicación de las enfermedades venéreas. *Bol. Ofic. sanit. pan-amer.* **31**, 169 (Editorial)

REIN, C. R.
Problemas en el serodiagnóstico de la sífilis. *Bol. Ofic. sanit. pan-amer.* **31**, 105

KITCHEN, D. K.
Penicilinoterapia moderna : desenvolvimiento; eficacia; reacciones. *Bol. Ofic. sanit. pan-amer.* **31**, 118

BREWER, F. A.
Los nuevos antibióticos en el tratamiento de las enfermedades venéreas. *Bol. Ofic. sanit. pan-amer.* **31**, 127

SANCHEZ PEREZ, R.
Epidemiologia de las enfermedades venéreas. *Bol. Ofic. sanit. pan-amer.* **31**, 132

STOUT, G. W. & REYNARD, R.
Primera encuesta serológica centroamericana. *Bol. Ofic. sanit. pan-amer.* **31**, 141

SAMAME, G.
Organización de una división de control de las enfermedades venéreas. *Bol. Ofic. sanit. pan-amer.* **31**, 151

1952

SAMAME, G.
Programas de control de las enfermedades venéreas de la Oficina Sanitaria Panamericana, Oficina Regional de la Organización Mundial de la Salud. *Bol. Ofic. sanit. pan-amer.* **32**, 37

STOUT, G., GUZMAN, M. & SCRIMSHAW, N. S.
Reacciones serológicas para sífilis presuntamente positivas falsas en la América Central. I. Incidencia y distribución. *Bol. Ofic. sanit. pan-amer.* **32**, 206

Reacciones serológicas para sífilis presuntamente positivas falsas en la América Central. II. Relación con el ácido ascórbico, riboflavina, fosfatasa alcalina, carotina y vitaminas A y E en el suero sanguineo. *Bol. Ofic. sanit. pan-amer.* **32**, 521

REIN, C. R., KITCHEN, D. K., MARQUEZ, F. & VARELA, G.
Penicilina de acción retardada en el tratamiento del mal del pinto en el campesino mexicano : estudio clínico y serológico. *Bol. Ofic. sanit. pan-amer.* **33**, 95

BAUER, T. J.
Tratamiento y control modernos de las enfermedades venéreas. *Bol. Ofic. sanit. pan-amer.* **33**, 105

STOUT, G., MENDEZ, J. & GUZMAN, M.
Reacciones serológicas para sífilis presuntamente positivas falsas en la América Central. III. Relación con el contenido de proteina, albumina y globulina en el suero. *Bol. Ofic. sanit. pan-amer.* **33**, 110

GAYOSO, P. C.
Métodos modernos de control de las enfermedades venéreas. *Bol. Ofic. sanit. pan-amer.* **33**, 116

FUNES, J. M. & AGUILAR, C. LUZ
La solución de mafarside-orvus en la profilaxis de la blenorragia en la mujer. *Bol. Ofic. sanit. pan-amer.* **33**, 121

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Naturaleza y extensión del problema del pian en las Américas. *Bol. Ofic. sanit. pan-amer.* **33**, 126

GOODMAN, H.
Método para vencer la renuencia de los enfermos venéreos a revelar sus contactos. *Bol. Ofic. sanit. pan-amer.* **33**, 142

SIMPSON, W. G. & MURPHY, V.
Necesidad de mejorar la formación profesional de las enfermeras de venereologia. *Bol. Ofic. sanit. pan-amer.* **33**, 146

1953

BONNE, W. M., GUTHE, T. & REYNOLDS, F. W.
El Papel de la Organización Mundial de la Salud en el control del pian. *Bol. Ofic. sanit. pan-amer.* **34**, 340

EDMUNDSON, W. F.
Control antivenéreo por la aplicación profiláctica de penicilina a grupos muy expuestos. *Bol. Ofic. sanit. pan-amer.* **34**, 347

GUIMARÃES, F. N.
El pian en Brasil. *Bol. Ofic. sanit. pan-amer.* **34**, 468

ROBERTS, P. W.
Informe clínico sobre el empleo de la penicilina en el tratamiento de 100 casos de mal de pinto. *Bol. Ofic. sanit. pan-amer.* **34**, 542

SALAS, A. C.
Control de las enfermedades venéreas en la zona fronteriza Mexicana-Estadounidense. *Bol. Ofic. sanit. pan-amer.* **35**, 124

GUEVARA, J. A. & MASI, D. A.
Control de las enfermedades venéreas en el Paraguay. *Bol. Ofic. sanit. pan-amer.* **35**, 132

HILL, K. R.
Tratamiento del pian con antibióticos distintos de la penicilina. *Bol. Ofic. sanit. pan-amer.* **35**, 147

EDMUNDSON, W. F., RICO, A. L. & OLANSKY, S.
Estudio clinicoserológico del mal de pinto. *Bol. Ofic. sanit. pan-amer.* **35**, 163

Monographs

HILL, K. R., KODIJAT, R. & SARDADI, M.
Atlas of framboesia (*World Health Organization : Monograph Series* No. 5; also published in *Bull. Wld Hlth Org.* 1951, **4**, 201)

PANGBORN, M. C., MALTANER, F., TOMPKINS, V. N., BEECHER, T., THOMPSON, W. R. & FLYNN, M. R.
Cardiolipin antigens (*World Health Organization : Monograph Series* No. 6 ; also published in *Bull. Wld Hlth Org.* 1951, **4**, 151)

GRIN, E. I.
Epidemiology and control of endemic syphilis : report on a mass-treatment campaign in Bosnia (*World Health Organization : Monograph Series* No. 11 ; also published in *Bull. Wld Hlth Org.* 1952, **7**, 1)

WORLD HEALTH ORGANIZATION
First International Symposium on Yaws Control (*World Health Organization : Monograph Series* No. 15; also published in *Bull. Wld Hlth Org.* 1953, **8**, 7-390)

Reports of Experts and Study Groups

Expert Committee on Venereal Infections and Treponematoses
First Report (*Official Records of the World Health Organization*, 1948, **8**, 60)
Second Report (*Official Records of the World Health Organization*, 1949, **15**, 18)
Third Report (*World Health Organization : Technical Report Series*, 1950, **13**)
Fourth Report (*World Health Organization : Technical Report Series*, 1953, **63**)

Expert Committee on Venereal Infections and Treponematoses, Subcommittee on Serology and Laboratory Aspects
First Report (*World Health Organization : Technical Report Series*, 1950, **14**)
Second Report (*World Health Organization : Technical Report Series*, 1951, **33**)

Venereal-disease control in the USA : report of the WHO Syphilis Study Commission (*World Health Organization : Technical Report Series*, 1950, **15**)

Special Publications

International List of Venereal-Disease Treatment Centres at Ports
Personal Booklet (issued to seamen for recording treatment of venereal disease at ports)

Chronicle of the World Health Organization

1948

Venereal diseases : an international problem. *Chron. Wld Hlth Org.* **2**, 15
New international effort against venereal diseases. *Chron. Wld Hlth Org.* **2**, 267

1949

Serology of syphilis. *Chron. Wld Hlth Org.* **3**, 14
Penicillin in venereal diseases. *Chron. Wld Hlth Org.* **3**, 15
Venereal-disease control in Poland. *Chron. Wld Hlth Org.* **3**, 29
Venereal diseases in Ethiopia. *Chron. Wld Hlth Org.* **3**, 83
Venereal disease in Germany. *Chron. Wld Hlth Org.* **3**, 111
Venereal-disease control among Rhine River boatmen. *Chron. Wld Hlth Org.* **3**, 117
Penicillin treatment of syphilis. *Chron. Wld Hlth Org.* **3**, 285

1950

New developments in venereal-disease control. *Chron. Wld Hlth Org.* **4**, 35
Serology of syphilis. *Chron. Wld Hlth Org.* **4**, 41
Venereal-disease control in the USA. *Chron. Wld Hlth Org.* **4**, 67
International conference on the serodiagnosis of syphilis. *Chron. Wld Hlth Org.* **4**, 150
Lymphogranuloma venereum. *Chron. Wld Hlth Org.* **4**, 345
Serology of syphilis. *Chron. Wld Hlth Org.* **4**, 367

1951

Symposia on syphilis. *Chron. Wld Hlth Org.* **5**, 9
Anti-Venereal-Disease Commission for Rhine River Area. *Chron. Wld Hlth Org.* **5**, 72
Cardiolipin antigens. *Chron. Wld Hlth Org.* **5**, 265

1952

Venereal-disease-control demonstration in India. *Chron. Wld Hlth Org.* **6**, 90
First International Symposium on Yaws Control. *Chron. Wld Hlth Org.* **6**, 253
Mass treatment of syphilis in an Indian province. *Chron. Wld Hlth Org.* **6**, 266
The International Treponematosis Laboratory Center. *Chron. Wld Hlth Org.* **6**, 290
A rapid method for the serodiagnosis of syphilis. *Chron. Wld Hlth Org.* **6**, 301

1953

Endemic syphilis in Bosnia. *Chron. Wld Hlth Org.* **7**, 4
Venereal-disease-control demonstration in Egypt. *Chron. Wld Hlth Org.* **7**, 142
Venereal infections and treponematoses. *Chron. Wld Hlth Org.* **7**, 147
Report of the study-group on syphilis at the Sixth World Health Assembly. *Chron. Wld Hlth Org.* **7**, 203

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